Implementation and Scale-up Plan for GeneXpert Network in Bangladesh

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ACRONYMS

AFB	Acid fast bacilli
AIDS	Acquired Immunodeficiency Syndrome
BAB	Bangladesh Accreditation Board
CDC	Centers for Disease Control and Prevention
CDC	Chest Disease Clinics
CPC	Cetylpyridinium Chloride
DF	Damien Foundation
DGHS	Directorate General of Health Services
DRS	Drug Resistance Survey
DST	Drug sensitivity test
EQA	External quality assessment
EPZ	Export processing zone
FIND	Foundation for Innovative New Diagnostics
GLI	Global Laboratory Initiative
HEED	Health, Education, Economic development
HIV	Human Immunodeficiency Virus
ITM	Institute of Tropical Medicine
LED FM	Light-emitting diode fluorescence microscopy
LPA	Line probe assay
M&E	Monitoring and evaluation
MDR-TB	Multidrug-resistant tuberculosis
MSH	Management Sciences for Health
MOHFW	Ministry of Health and Family Welfare
MTB	Mycobacterium tuberculosis
NFM	Global Fund New Funding Model
NTRL	National TB reference Laboratory
RTRL	Regional TB reference Laboratory
PEPFAR	US President's Emergency Plan for AIDS Relief
PLHIV	People living with HIV/AIDS
PT	Proficiency testing
QA	Quality assurance
QC	Quality control
RIF	Rifampicin
SOP	Standard Operating Procedure
SWOT	Strengths, weaknesses, opportunities, and threats
TB	Tuberculosis
TWG	Technical Working Group
USAID	US Agency for International Development
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

FOREWORD

The adoption of the Xpert® MTB/RIF test Rollout and Implementation Plan by the Ministry of Health and Family Welfare (MOHFW) in Bangladesh marks a big step forward. It underscores the program's commitment to providing the latest in rapid testing technology for tuberculosis (TB) in Bangladesh in line with the End TB Strategy. Earlier TB detection, including smear-negative disease often associated with HIV/TB co-infection and young age, as well as expanded capacity to diagnose multidrug-resistant tuberculosis (DR-TB) are global priorities for TB control. DR-TB poses a formidable challenge due to its complex diagnostic and treatment requirements, while HIV-associated TB goes largely undetected due to the limitations of current diagnostic techniques. Conventional laboratory methods are slow and cumbersome, and novel technologies for rapid detection are therefore the focus of TB research and development laboratories. As such, the GeneXpert MTB/RIF test has been approved and policy recommendations issued by the WHO early in 2011. The Xpert MTB/RIF assay - an automated molecular diagnostic test with a simple, rapid and highly sensitive MTB/RIF diagnostic tool - and upcoming ULTRA cartridge should be deployed as close as possible to the point of patient care in the fight against TB.

The implementation plan provides guidance on the rollout of the Xpert MTB/RIF test, and in collaboration with World Health Organization and partners, details best-practice for its use as a rapid diagnostic test for TB & DR-TB across the tiers of the healthcare system.

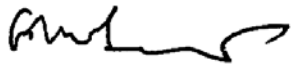
In 2015, WHO estimated, across all ages and forms of the disease, that TB in Bangladesh has an incidence of 225 (95% CI: 146-321) and a prevalence of 382 (95%CI: 185-647) per 100,000. These estimates are based on notification data, along with expert opinion on under-notification in Bangladesh. These WHO estimates will be updated based on results from a recently completed TB prevalence survey.

The standardization of approaches in the diagnosis and clinical care of TB patients in both the private and public health sectors, and ensuring consistent provision of high-quality services by all health care providers, are essential to preventing DR-TB.

The Ministry of Health and Family Welfare (MOHFW), along with the government, are committed to intensifying efforts to prevent and control TB, as well as to care for those affected by it in collaboration with development partners and other stakeholders.

I take this opportunity to express my sincere appreciation and gratitude to our partner Management Sciences for Health through the USAID-funded Challenge TB project for their contribution to the development of this implementation plan and for their continuing financial and technical support.

It is my sincere hope that all partners and health workers will find this implementation plan useful in their daily work and that the information contained herein will stimulate a renewal of the spirit of commitment and dedication to improve the quality of services provided for the people of Bangladesh.



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The development of the implementation and scale up plan for GeneXpert Network with budget is an expression of the commitment by the NTP, NTRL, Regional TB Reference laboratory, and its development partners for a strengthened TB, HIV and DR-TB response in Bangladesh. The Ministry of Health would like to acknowledge the following experts for their contribution and commitment in the development of this implementation and scale up plan.

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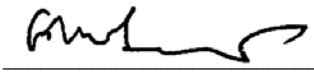

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RATIONALE FOR AN IMPLEMENTATION AND SCALE –UP PLAN

Elimination of tuberculosis (TB) is a major global health priority. Multidrug-resistant tuberculosis (MDR-TB) and HIV-associated TB pose enormous challenges to the health system due to the complexity of diagnosis and treatment. The End TB strategy underscores the urgent need for rapid diagnosis and universal access to DST to control TB, especially in resource-limited settings.

In 2010, the World Health Organization (WHO) endorsed a real-time polymerase chain reaction (PCR) based molecular test - the Xpert MTB/RIF assay - which Cepheid developed to detect *Mycobacterium tuberculosis* (MTB) and rifampicin resistance. This automated, fully-integrated system enables molecular testing in settings with high TB burden, providing results within 90 minutes. With its ease of use, this system can be adopted in district and sub-district settings, where the impact of testing on the clinical decision-making process is greatest.

The overall objective of this implementation plan is to define the strategy for implementation of the Xpert MTB/RIF test for rapid detection of TB and rifampicin (RIF) resistance in Bangladesh, within the context of the National Tuberculosis Program (NTP) strategic plan and other national health guidelines. It is intended to serve as the main guiding document for national, regional and local program managers, clinicians, coordinators, laboratories and their staff, donors involved in TB control, local and national implementing partners, as well as other health workers.

The two major objectives for Xpert MTB/RIF test implementation in Bangladesh are as follows:

- To utilize the Xpert MTB/RIF test to improve detection of TB and MDR-TB in line with the End TB strategy to access to universal DST;
- To roll out the Xpert MTB/RIF test so that there is at least one GeneXpert instrument per region (up to the district level). The target is to place 163 GeneXpert instruments in Bangladesh by 2018.

This plan provides a roadmap for internal and external support for Xpert MTB/RIF test rollout and implementation. This implementation plan fits within the overall policy framework provided by the following Bangladesh national policy documents:

- National TB Laboratory Strategic Plan (2018–2022)
- Bangladesh TB Laboratory strategic plan (2016-2020)

The MOHFW through the NTP management has appointed an Xpert MTB/RIF focal person responsible for leading implementation, and technical partners have been consulted and engaged on Xpert MTB/RIF implementation. The TB Laboratory Working Group (LWG), chaired by the NTP, has been convened and has validated all tools developed to monitor Xpert implementation and this implementation plan. The TB LWG will help to ensure that the work plan is updated according to country needs, new WHO policies, and experience over the five years of budgeted implementation.

OBJECTIVES AND BACKGROUND

In May 2014, the World Health Assembly approved the End TB Strategy, which proposes the ambitious target of ending the global TB epidemic by 2035. This goal will be met when TB-related deaths and active TB incidence are reduced by 95% and 90%, respectively, compared with the 2015 values. Are we on track to reach these goals?

Understanding TB diagnosis is critical to understanding why the world is currently failing to end TB. To treat a person with TB, one must first find and diagnose them. An estimated 41% of cases of active TB disease went undetected in 2015. This means that an estimated 4.3 million people went without proper TB care in 2015, leaving them ill, at risk of death, and with the potential to transmit disease to others. Closing this massive gap will require much better use of current diagnostic methods, as well as research into faster, simpler, more accurate, and less expensive options.

The Xpert® MTB/RIF test for the GeneXpert® platform (Cepheid Inc., Sunnyvale, CA, USA) is a fully automated nested real-time PCR system. It detects MTB's complex DNA, as well as MTB with rifampicin resistance-conferring mutations by identifying mutations in the *rpoB* gene in sputum and other sample types (*i.e.* pleural, lymph node aspirate or tissue, cerebrospinal fluid, gastric fluid and tissue other than lymph node). By fully integrating and automating all processes required for real-time PCR based molecular testing, the Xpert MTB/RIF test represents a simple and robust molecular test suitable for use in resource-limited settings, where TB burden is highest, and is able to provide results directly from sputum within 2 hours. Attaining equitable access to rapid, high-quality TB diagnosis and treatment necessitates the expansion of diagnostic testing. Balancing centralized with decentralized testing to gain maximum efficiency and coverage depends on a range of factors and varies across country, region and facility. For health systems where strong laboratory referral networks are already in place, the appropriate choice may be to strengthen sample referral. In cases where sample referral is weak but linkage to care is strong, there may be a preference for decentralization of Xpert MTB/RIF assay capacity to district and sub-district levels.

The introduction and scale-up of new tools for the diagnosis of TB has the potential to make a huge difference in the lives of people in Bangladesh and to help reach the target set up in the NSP (2018-2022) in line with the End TB strategy. To apply these tools most effectively, policymakers need information to make the right decisions about which new tools to implement and where in their national diagnostic algorithms to apply them. A technological breakthrough such as the Xpert MTB/RIF test is quite important for countries with high rates of TB and MDR TB - such as Bangladesh, which have MDR-TB rates of 1.6% and 29% MDR in new and retreatment cases, respectively. During Global Fund New Funding Model (NFM) implementation, the NTP received results from pilot projects in multiple areas in which all cases were tested with GeneXpert. The empirically observed figures are significantly different from those that could be expected on the basis of the DRS results. On average, the actually observed MDR level is 0.21% in new cases, and 29% in retreatment cases. The NTP will conduct another DRS in 2017, and the results of that study will be used to update the projected number of MDR-TB cases.

This represents a substantial under-diagnosis of MDR-TB cases in the country, contributing to poor patient outcomes and further spread of the disease.

In adults thought to have TB, with or without HIV infection, the Xpert MTB/RIF test is sensitive and specific. Compared with smear microscopy, the Xpert MTB/RIF test substantially increases TB detection among culture-confirmed cases. Results of a recent meta-analysis of MTB/RIF as an initial test replacing smear microscopy are summarized in Table 1 below. The Xpert MTB/RIF test has the potential to revolutionize TB diagnostic capability for clinicians managing the disease, and to transform the usual lengthy pathway to diagnosis and treatment for those with MDRTB.

Table 1: Meta-analysis of MTB/RIF

Type of analysis	No. of studies	No. of participants	Median (%) pooled sensitivity (95% Confidence Interval)	Median (%) pooled specificity (95% Confidence Interval)
Xpert MTB/RIF used as an initial test for TB detection replacing smear microscopy	22	8,998 (2,953 confirmed TB, 6,045 non-TB)	89 (85–92)	99 (98–99)
Xpert MTB/RIF used as an add-on test for TB detection following a negative smear-microscopy result (people with HIV infection)	7	1,789	79 (70–86)	99 (98–99)
Xpert MTB/RIF used as an add-on test for TB detection following a negative smear-microscopy result (people without HIV infection)	7	1,470	86 (76-92)	
Xpert MTB/RIF used as an initial test for detecting rifampicin resistance replacing conventional drug-susceptibility testing as the initial test (41 studies, 2966 participants),	41	2,966 (555 refampicin-resistance positives; 2,411 negatives)	95 (90–97)	98 (97–99)

Recent publication on ULTRA has shown more improvement of the Xpert cartridge, as sensitivity of the Ultra was 5% higher than that of Xpert (95%CI +2.7, +7.8) but specificity was 3.2% lower (95%CI -2.1, -4.7). Sensitivity increases were highest among smear-negative patients (+17%, 95%CI +10, +25) and among HIV-infected patients (+12%, 95%CI +4.9, +21). Specificity decreases were higher in patients with a history of TB (-5.4%, 95%CI -9.1, -3.1) than in patients with no history of TB (-2.4%, 95%CI -4.0, -1.3). Reclassifying 'trace-calls' (the semi-quantitative category of the Ultra assay that corresponds to the lowest bacillary burden) as 'TB-negative', either in all cases or in those with a history, mitigates most of the specificity losses (Specificity –1.0% and -1.9% if trace reclassified for all cases or only cases with TB history, respectively) while maintaining some of the sensitivity gains over Xpert (Sensitivity +7.6% and +15%). Ultra has higher sensitivity than Xpert particularly in smear-negative and HIV-infected patients and at least as good accuracy for RIF detection. However, as a result of the increased sensitivity, Ultra also detects non-viable bacilli present particularly in patients with recent history of TB.

However, the epidemiological context and the organization of the TB specific health system strongly determine the impact of the Xpert MTB/RIF test on case detection and/or time to diagnosis, and therefore need to be taken into consideration for strategic planning. It is also important to ensure adequate coordination for the sustainable introduction and rollout of the GeneXpert technology in the public and private health sector. For these reasons, this implementation plan has been developed as a subset of the NSP (2018-2022) and *National TB Laboratory Strategic Plan* (2016-2020) to provide a roadmap for Xpert MTB/RIF test implementation in Bangladesh.

SITUATIONAL ANALYSIS

EPIDEMIOLOGICAL DATA

With an estimated population of 157 million Bangladesh is one of 22 high TB and 27 MDR-TB burden countries. WHO estimated the incidence and prevalence for all ages and all forms of TB in 2015 in Bangladesh to be 225 (95% CI: 146-321) and 382 (95%CI: 185-647) per 100,000 (Table 2). These estimates are based on notification data together with expert opinion regarding under-notification in Bangladesh. These WHO estimates will be updated based on results from a recently completed TB prevalence survey.

Table 2: WHO estimates of TB burden 2016

Estimates of TB Burden 2016*	Number (thousands) [confidence interval (CI)]	Rate (per 100,000 population) [CI]
Mortality[1]	66 [43-94]	40 [26-58]
Incidence[2]	360 [262-474]	221 [161-291]
Prevalence (all ages all forms)		295
Incidence (MDR/RR-TB)	8.8 [4.8-13]	5.4 [2.97.8]

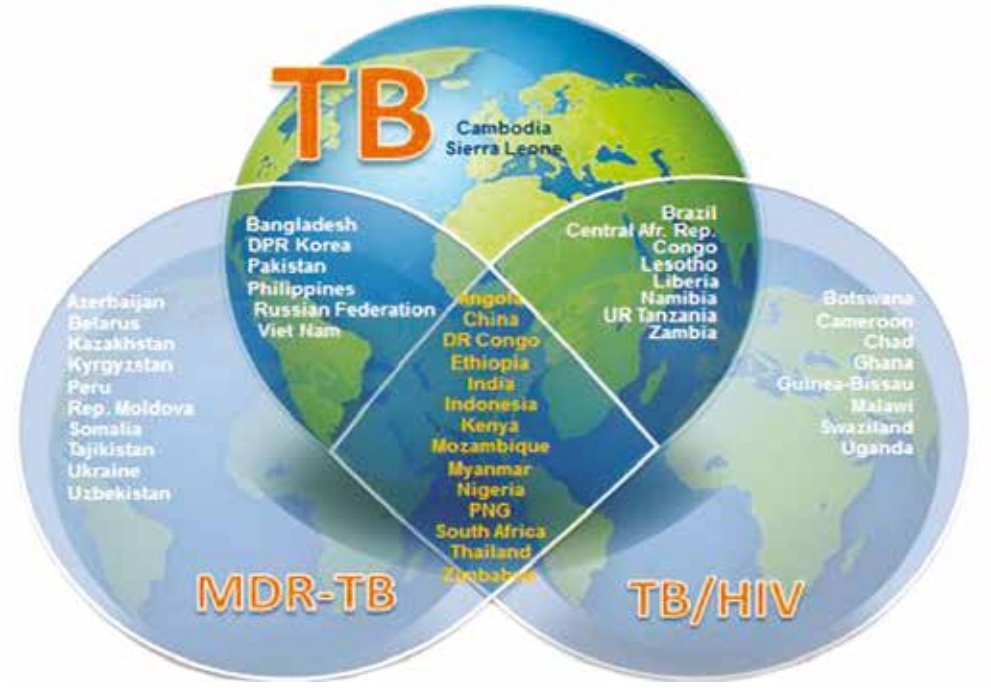
Source: Global TB Report 2017

1. Excludes HIV positive TB

2. Includes HIV Positive TB

*ranges represent uncertainty intervals

Figure1. Tuberculosis High burden countries, WHO 2016



Bangladesh prevalence survey (2016)

The recent survey of 98,710 participants, conducted between 2015 and 2016, was designed in accordance with WHO standards. The participation rate was high, though higher among women (93.3%) than men (87.8%) and lowest for men in the 25 to 34 age group. Participation was also lower in urban settings.

Overall 20,594 (21%) participants screened positive through a symptom screen and/or chest X-ray, of which 20,463 (99.4%) submitted sputum samples for laboratory diagnostic testing. Laboratory tests confirmed 291 TB cases (92% confirmed by GeneXpert and 53% confirmed by culture).

The prevalence figures for bacteriologically confirmed TB and smear positive TB were estimated to be 295 (95%CI: 247-344) and 110 (95% CI: 85-135) per 100,000 adults, respectively.

HIV-associated TB

Bangladesh has localized HIV cases with a prevalence of about 0.1% in the general adult aged 15-49 population, though it is substantially higher in key populations. Testing TB cases for HIV is not routinely done in Bangladesh. Therefore, the number of TB patients known to be HIV+ comes from the HIV testing of certain risk groups including:

- TB cases with history of high risk behaviour
- Complicated extrapulmonary TB, Relapse and treatment failure cases
- Drug resistant TB
- Clinical suspects of HIV infection
- Children of mother known to be HIV positive

The country profile for Bangladesh in 2016, reported by the country to WHO, states that of TB patients tested, 87 (12.5%) tested positive for HIV.

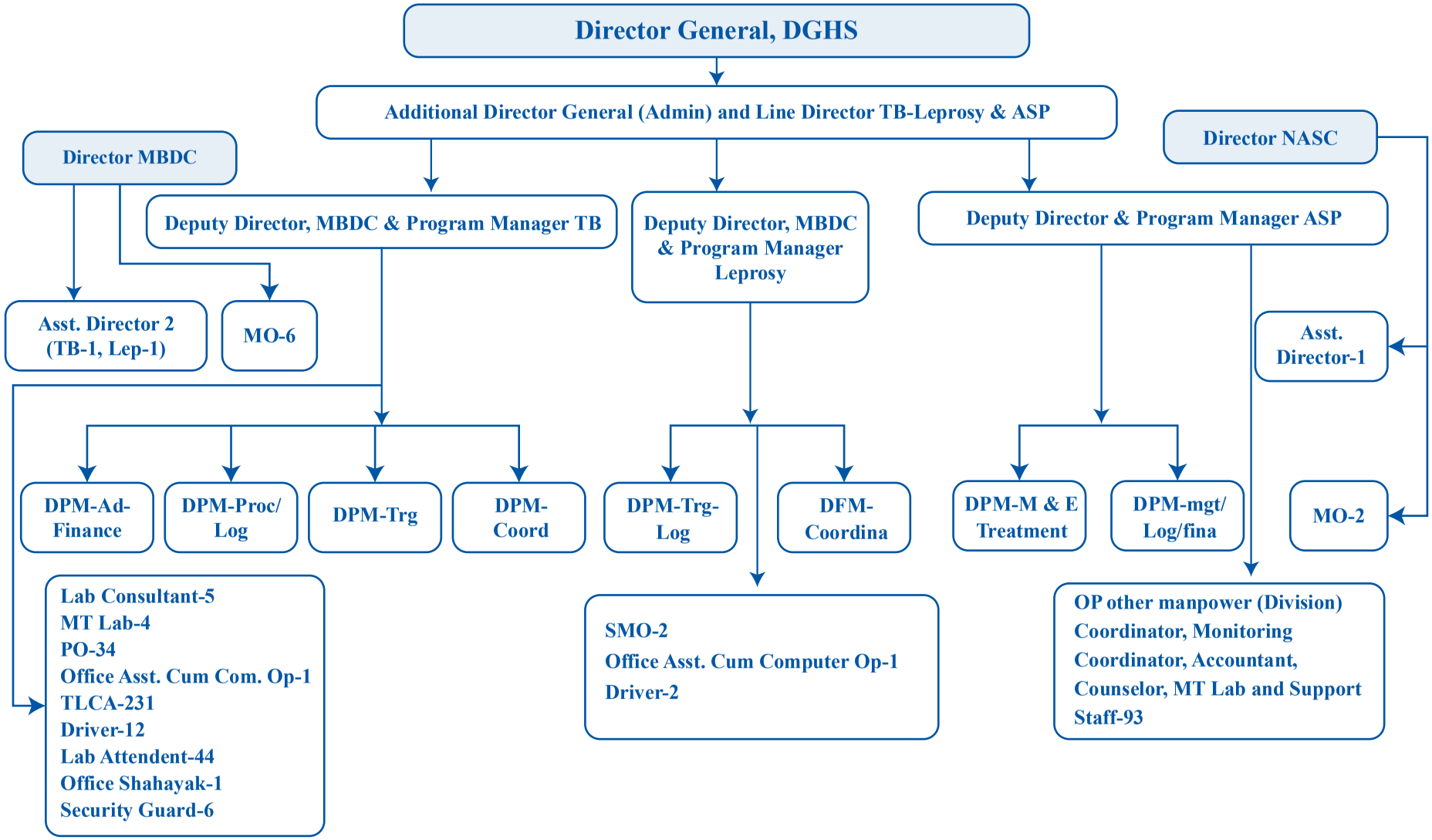
A recent review of the NTP (2016) identified the following gaps in the diagnosis of TB and MDR-TB in the country:

- Coverage with new diagnostic technologies has remained incomplete
- More than 40% of all TB cases and more than 80% of MDR-TB cases are still undiagnosed
- Low usage of the GeneXpert instrument capacity
- Lack of linkage to care in rifampicin resistant TB cases identified by the Xpert MTB/RIF test
- Lack of antiretroviral therapy (ART) initiation in TB-HIV co-infected cases
- Successful active case finding activities at a community level have not yet been expanded to cover the whole country
- The engagement of individual private practitioners and public/private hospitals has remained limited, and mandatory TB case notification is yet to be operationalized
- Coordination of the TB response in urban areas is weak
- Childhood TB detection and management is largely insufficient
- Electronic recording/reporting systems have not yet reached full coverage
- The TB response remains highly dependent on external funding

LABORATORY SWOT ANALYSIS

The TB laboratory network is an integral part the National TB Control Program (NTP) which is under the directorate of “Mycobacterial Disease Control”. This directorate in turn functions under DGHS (Directorate General of Health Services) of the Ministry of Health and Family Welfare).

Figure 2: Directorate General of Health Services



Note that this organogram will be revised due to new appointment and positions created by MOHFW in April 2017.

Though significant improvements have been made in recent years, the laboratory network in Bangladesh still faces many challenges. The primary issues were captured in the strengths, weaknesses, opportunities, and threats (SWOT) analysis (**Figure 3**) conducted as part of the development of the *National TB Laboratory Strategic Plan (2016-2020)*.

Figure 3: SWOT analysis

Strength

- NTP strategic plan 2018-2022 includes expansion of TB laboratory network to 1 microscopy center /100 000 population and replace ZN microscopy with LED FM in all sub-districts by 2020
- TB laboratory network has a well-defined four level structure
- TB laboratory strategic plan (2016-2020) developed
- Four functional culture labs (NTRL and three RTRLs)
- Molecular diagnostics (Xpert MTB/RIF) available at 51 machines in 47 sites and plan for expansion to 296 machines in 2020s; LPA technique is implemented at NTRL
- Good laboratory infrastructure at the NTRL
- All guidelines available and enough HR at NTRL supported by GOB and partners

Main weaknesses

- Low coverage of TB microscopy (including LED FM), culture and DST according to WHO targets
- Low performance of microscopy centers
- TB lab network is not fully functional (regional labs are not involved in supervision)
- Infrastructure and safety measures in many TB microscopy and some regional labs are not up to standards
- Infrastructure at NTRL requires renovation
- Some labs are overloaded
- Xpert training quality is not up to standards
- Maintenance of TB lab equipment is a major problem at all levels of the network including routine prevention and repair
- NTRL and RTRLs do not have laboratory informational system

Main opportunities

- Strong commitment of NTP and partners to strengthening TB laboratory network
- Availability of structure and infrastructure at all level of MOHFW
- Availability of private laboratories
- Availability of government posts for sub-district laboratories
- Availability of international tools, material, training and technical assistance capacity
- Existing pool health workers and community management volunteers for specimens collection and transportation
- Existence of courier services
- Increased focus on TB operational research and existing governmental OR budget line
- Existing national hospital waste management regulations

Main threats

- Dependence on donor support
- Potentially limited funding to implement planned activities, coupled with untimely disbursement of funds
- Lack of in-country capacity for maintenance and repair of lab equipment
- Lack of national regulations for laboratory services
- Inadequate coordination between NTP and partners
- High staff turnover, lack of retention policy for trained staff
- Safety risk to laboratory staff handling specimens with minimal safety measures
- Insufficient HR capacity for TB lab commodities procurement
- Lack of donor support for construction of new buildings

The plan calls for the establishment of strong and decentralized microscopy and Xpert laboratories, which will mark a significant shift in the structure of laboratory services in Bangladesh.

NTP plans to increase detection of all forms of TB to 280, 933 in 2020 from 218,000 in 2016. According to the national strategic plan (NSP, 2018-2022) the number of diagnostic facilities will be increased to reach the target of 1 microscopy centre per 150 000 people.

The country has a laboratory network that is partially established at four levels, in harmony with the general health system (National, Regional, District and Peripheral). Smear microscopy is the primary tool for diagnosis of TB in the country with functional EQA, with both ZN and FM microscopy services being available. GeneXpert services were introduced in 2012 and are being scaled up. Quality assured culture & DST and rapid molecular diagnostic services are available at NTRL Dhaka (solid and liquid culture & 1st/2nd line LPA) and in 4 Regional reference laboratories (Chittagong, Khulna, Rajashahi and Sylhet). In addition, a quality assured Culture and DST laboratory is functional at Netrakona supported by Damien Foundation and WHO supranational Reference laboratory at Antwerp.

There are 1,150 microscopy laboratories all over Bangladesh under NTP, with 700 light microscopes and 450 LED fluorescence microscopes (LED-FM) providing services throughout the country. Currently there are no private laboratories in the quality-assured microscopy network, though there are private laboratories providing smear microscopy services. The laboratory consumables/reagents for microscopy services are of good quality and supplies are uninterrupted.

The smear microscopy network is quality assured by 40 EQA laboratories which supervise and perform blinded rechecking based on a national sample (five slides per months from each microscopy center) using the WHO EQA guidelines. Microscopy EQA coverage by rechecking has been close to 100% and is being conducted systematically. The workload for first controllers appears to be quite high, with some EQA centers supervising as many as 60 microscopy diagnostic centers. LED FM has been introduced and is being scaled up with 440 lab technicians trained across the country.

There is one NTRL physically situated in the National Institute of Infectious Diseases and Chest Hospital (NIDCH), the organization from which the head of the NTRL is seconded. The facility has functional solid and liquid culture, GeneXpert, and LPA. Second line LPA is being standardized for PMDT services and has been available from Jan 2017 to assist with the introduction of the shorter MDR TB regimen.

Table 3. Summary of TB testing facilities in Bangladesh[a]

TB Test	Number of facility test is available
Sputum smear microscopy [b] (diagnostics centres)	Available at 1,150 diagnostic centres, district/ sub-district levels. TOTAL for clinical use: [700 lights centre and 450 LED FM]
TB culture: Solid/ Liquid culture / DST [c]	Available at NTRL Laboratory in Dhaka 4 Regional reference laboratories : Chittagong, Khulna, Rajashahi, and Sylhet TOTAL for clinical use: [4]
LPA	Available at NTRL Laboratory in Dhaka
Rapid detection of TB or drug resistant TB (Xpert MTB/RIF test)	163 Xperts are operational throughout the country

[a] NTP internal data, April 2017

[b] Ziehl Neelsen, fluorescence microscopy- conventional vs. LED, direct vs. concentrated

[c] DST: first line DST by conventional methods, e.g. direct or indirect test; solid or liquid culture, drugs tested, concentration of drugs tested;; proportion, absolute concentration or resistance ratio method; second line DST by conventional methods, e.g. solid culture medium, drugs tested, concentration of the drugs; rapid detection of TB or drug resistant TB. e.g. Xpert MTB/RIF test

GROUPS ELIGIBLE TO RECEIVE XPERT MTB/RIF TESTING

GeneXpert MTB/RIF testing is recommended by NTP as a first test for risk groups, to detect TB and resistance to RIF. Symptomatic (longer than 3 weeks of coughing, weight loss, and night sweats) smear negative individuals are also eligible for Xpert MTB/RIF testing without regard to HIV status.

163 GeneXpert instruments are currently operating in the NTP network (of which 155 machines have 4 modules, and 8 machines have 16). In addition to 163 Xperts 30 more instruments are used by private sector labs and other institutions supported by icddr,b. NTP plans to expand its network of Xpert machines to all districts, Major medical college hospitals and all upazilas (total 650 Xpert sites) by 2022.

Policy and objectives:

- The NTP will implement Xpert MTB/RIF/ULTRA Xpert testing for all presumptive TB and presumptive DR-TB cases in Bangladesh in adults and children, irrespective of HIV status;
- The NTP will roll out GeneXpert instruments in a phased manner to enable equitable access to testing in all districts of the country.

The MOHFW adopted the WHO recommendations for the use of Xpert MTB/RIF in the diagnosis of HIV-associated TB and MDR-TB. WHO recommends the following policy on the use of Xpert MTB/RIF to diagnose pulmonary TB and rifampicin resistance in adults and children:

- *Xpert MTB/RIF should be used, rather than conventional microscopy, culture and drug sensitivity test (DST), as the initial diagnostic test in adults presumptive of DR-TB or HIV associated TB (strong recommendation, high-quality evidence);*
- *Xpert MTB/RIF should be used, rather than conventional microscopy, culture and DST, as the initial diagnostic test in children presumptive of DRTB or HIV-associated TB (strong recommendation, very low-quality evidence);*
- *Xpert MTB/RIF may be used, rather than conventional microscopy and culture, as the initial diagnostic test in all adults having TB (conditional recommendation acknowledging resource implications, high-quality evidence);*
- *Xpert MTB/RIF may be used, rather than conventional microscopy and culture, as the initial diagnostic test in all children suspected of having TB (conditional recommendation acknowledging resource implications, very low-quality evidence);*
- *Xpert MTB/RIF may be used as a follow-on test to microscopy in adults suspected of having TB who are not at risk of MDR-TB or HIV-associated TB, especially when further testing of smear-negative samples is necessary (conditional recommendation acknowledging resource implications, high-quality evidence)*

A WHO Technical Expert Consultation in March 2017 on '*Non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF'* advised below Ultra implementation considerations

Figure 4: Ultra cartridge

The Ultra assay is non-inferior to the current Xpert MTB/RIF assay for the diagnosis of MTB and the detection of rifampicin resistance and can be used as an alternative to the current in all settings; Cepheid plans to gradually phase out and replace the current Xpert MTB/RIF assay with the Ultra assay. WHO's recommendations for the use of Xpert MTB/RIF also apply to the use of Ultra as the initial diagnostic test for all adults and children with signs and symptoms of TB and in the testing of selected extrapulmonary specimens (CSF, lymph nodes and tissue specimens). The following implementation considerations apply to Ultra:

- Ultra has high sensitivity for MTB detection and incorporates a new semi quantitative category "*trace call*" that corresponds to the lowest bacillary burden for MTB detection. Interpret "trace calls" as follows:
  - Among persons with HIV, children and extrapulmonary specimens "*trace calls"* should be considered to be true positive results for use in clinical decisions and patient follow-up;
  - Among persons not at risk for HIV, with an initial "*trace call*" positive result, a fresh specimen from the patient should undergo repeat testing and the result of the second Ultra test be used for clinical decisions and patient follow-up;
  - While clinical and available radiological information should always be considered in the diagnosis of tuberculosis, a second "*trace call"* positive is sufficient to make a diagnosis of pulmonary TB unless there is a recent history of TB;
  - Among all persons that test "*trace call*" positive additional investigations are needed to confirm or exclude resistance to rifampicin.
- The interpretations of Ultra results for MTB detection and Xpert MTB/RIF are otherwise the same
- Ultra has both high sensitivity and specificity for detection of rifampicin resistance.
  - The use of melting temperature based analysis with Ultra instead of real-time PCR analysis with Xpert MTB/RIF allows Ultra to better differentiate silent mutations from resistance conferring mutations;
  - In persons at low risk for rifampicin resistance (e.g. new TB cases not at risk for MDR-TB) a positive rifampicin resistance result should be repeated using a fresh specimen. Repeat testing is recommended to control for any pre-analytical and/or post analytical errors.
- All persons identified by Ultra as having rifampicin resistance should undergo further testing, as per current WHO policy guidance, to determine if there is additional resistance to the class of fluoroquinolones and/or the group of second-line injectable drugs.
- Ultra can be used on all GeneXpert instrument platforms and is suitable for use at central or national level reference laboratories, as well as at regional and district levels. GeneXpert has the potential to be used at the peripheral level, provided that uninterrupted electricity supply and temperature conditions can be ensured.

The MOHFW has determined that Xpert MTB/RIF testing will be implemented as the initial diagnostic test in all presumptive TB and presumptive DR-TB cases in adults and children. This includes:

- **All new TB cases presenting with presumptive TB**, irrespective of HIV status, *i.e.* PLHIV and those with negative and unknown HIV status
- **Presumptive DR-TB**.

The NTP manual defines the following patient groups as being at high risk for MDR-TB:

- Cases that have failed, relapsed, or returned after loss to follow-up and that were on a TB retreatment regimen (formerly chronic TB cases);
- Failure of the first line regimen (sputum smear positive cases at month five during the course of the standard treatment regimen for new TB cases);
- Relapses and returns after loss to follow-up from standard treatment for new smear positive cases at month 3 of retreatment;
- Symptomatic close contacts of a known MDR-TB patient

XPERT MTB/RIF TESTING ALGORITHM

The routine diagnostic algorithms for Bangladesh have been designed to maximize clinical outcomes and to assure appropriate instrument utilization, from Xpert sites to culture laboratories. It is of the utmost importance that all sites offering routine testing follow the national algorithm, and that all implementers are oriented and committed to following the policy.

Policy and objectives:

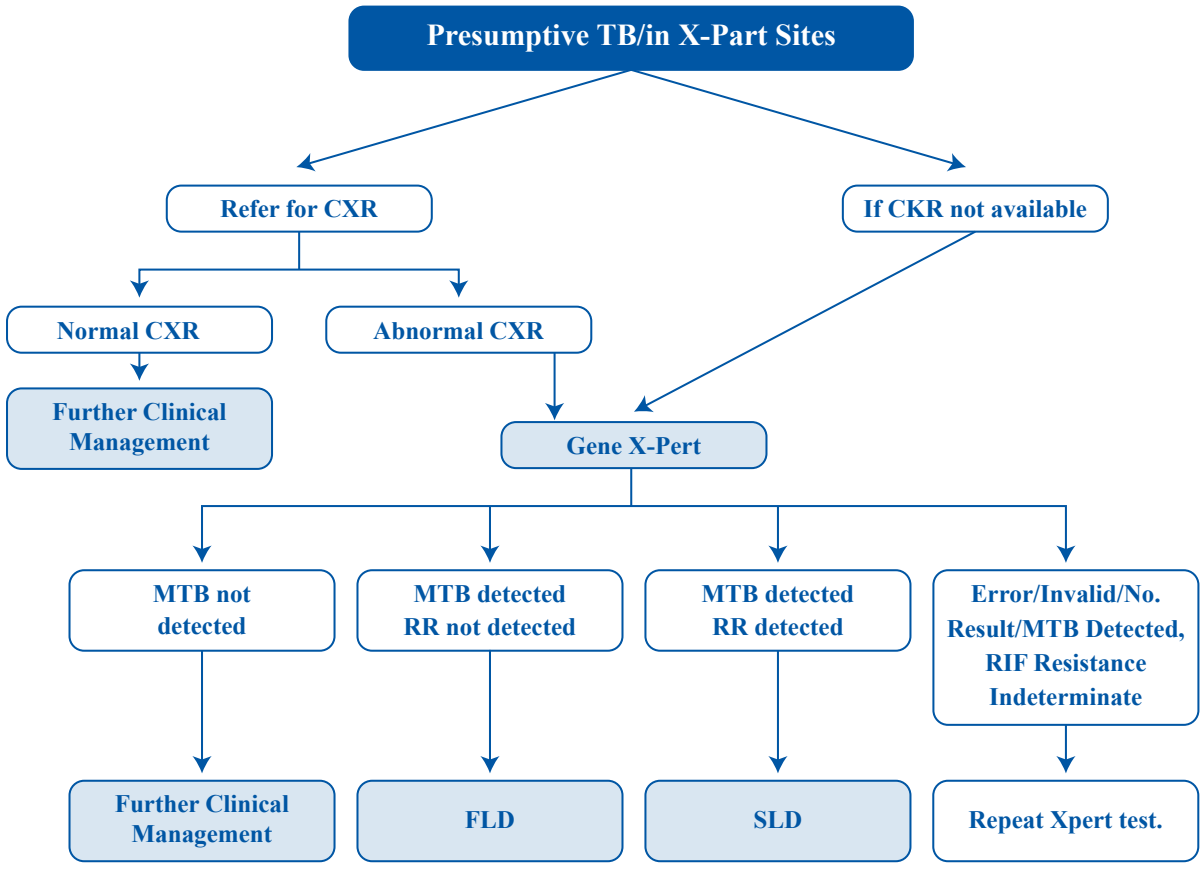
- The NTP will sensitize all institutions and implementing partners involved in Xpert MTB/RIF implementation on the national TB diagnostic algorithm
- The NTP will provide the training and tools required for implementation of the national TB diagnostic algorithm
- The NTP will confirm all Xpert MTB/RIF test rifampicin resistant cases using culture and DST for 1st and 2nd line and ensure all cases receive appropriate treatment

The NTP has developed the national TB diagnostic algorithm (**Figure 5**) that will ensure universal access to high quality TB, MDR-TB and HIV-related TB diagnosis. All implementation of Xpert MTB/RIF and upcoming ULTRA cartridge testing in the country should be done in accordance with the national TB diagnostic algorithm, and in close conjunction with the above NTP policy.

All testing sites offering Xpert MTB/RIF testing will follow the national TB diagnostic algorithm which later will be revised according to new ULTRA cartridge implementation. All implementing partners must commit to following these algorithms.

Smear positive pulmonary TB (PTB) cases are defined as patients with at least one positive smear with any number of AFBs detected. The definition of smear negative PTB is stratified into three possibilities depending on results of Xpert MTB/RIF testing (if available): symptomatic smear negative; Xpert positive/smear negative; and Xpert negative/chest X-ray (if available) consistent with active TB.

Figure 5: Proposed Algorithm for diagnosis and follow up of pulmonary tuberculosis

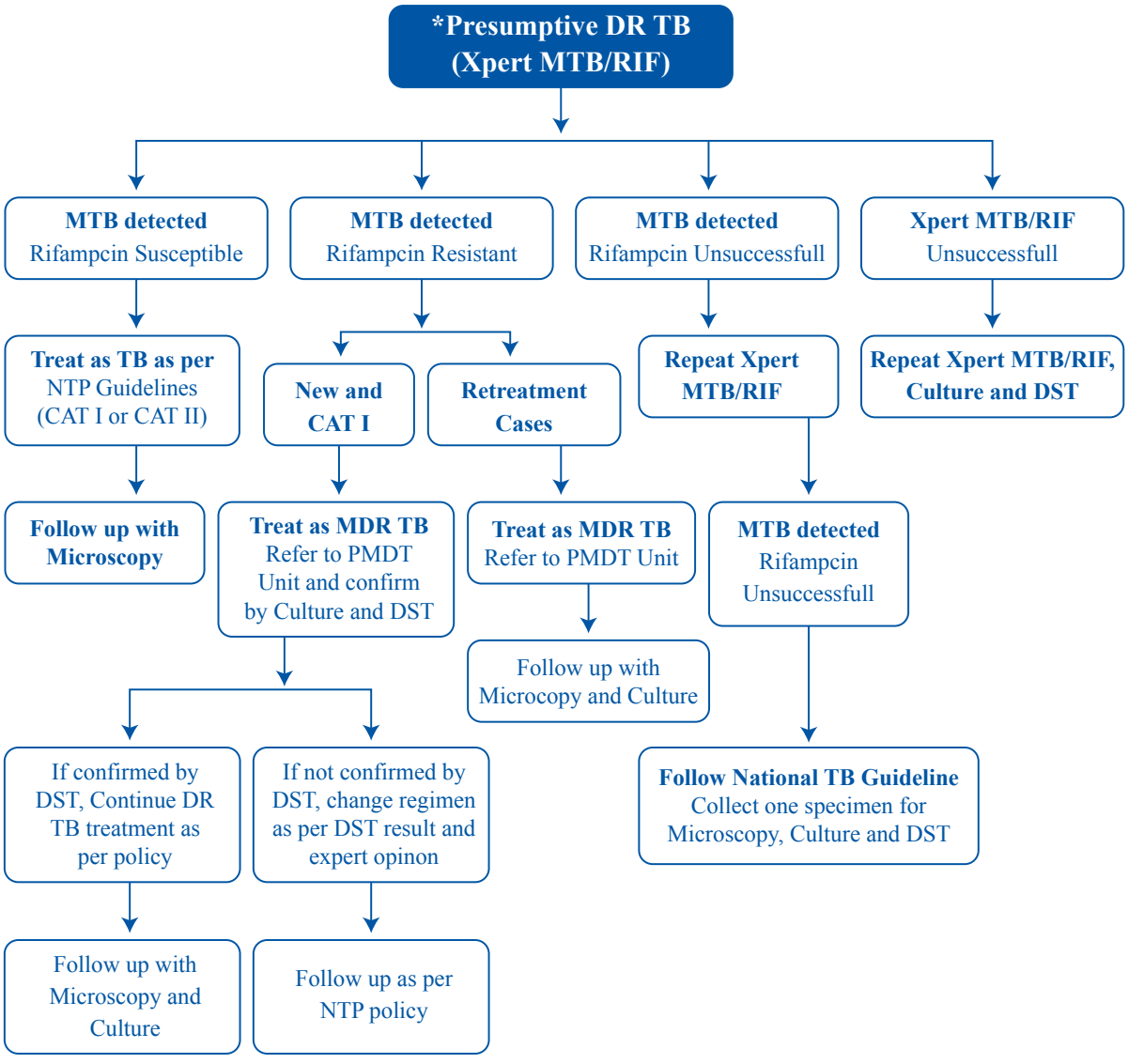


The NTP has recently assessed the efficacy and cost implications of various diagnostic algorithms. An NTP expert committee agreed that the use of the algorithm in Figure 5 would provide most benefits in terms of both case detection and cost implications.

The NTP plans to initiate this algorithm at the beginning of 2018, and expects to cover 134 sites throughout the year. During the NSP's implementation period (2018-2022), the NTP will procure additional Xpert machines to cover all upazillas, the CDC, Districts sadar hospitals, and most medical colleges by 2022. The performance of the new diagnostic algorithm will be evaluated in 2019, and then a decision on further scale-up or revision of the algorithm will be made based on this evaluation.

An algorithm (Figure 6) for diagnosis and follow-up of drug resistant tuberculosis was also developed for Xpert and non-Xpert sites.

Figure 6: Diagnostic algorithm for DRTB by Xpert MTB/RIF



***Presumptive DR TB Case:**

1. Failure of Category-I (remain positive at month 5 or later and smear negative patients with become smear positive at month 2
2. Failure of Category II (remain positive at month 5 or 8
3. Non converters of Category I (remain positive at month 2)
4. Non converters of Category II (remain positive at month 3)
5. Relapse (Category 1/Category II)
6. Treatment after loss to follow up (Category I/Category II)
7. Close contact of MDR TB patient with symptoms
8. HIV infected
9. Others (Specify.....)

Laboratory tests recommended for diagnosis of EPTB are: culture for body fluids and Xpert MTB/RIF, but not smear microscopy. Current laboratory practices for detection of TB in children are the same as those for adults. PLHIV are included in the priority group for testing by Xpert MTB/RIF (**Figure. 5**). Xpert MTB/RIF is recommended as a primary test for detection of drug resistant (DR) TB. Presumptive DR TB cases include previously treated TB patients, failures and non-converters of Cat I and Cat II treatment regimens, Cat I and Cat II lost to follow-up, symptomatic MDR TB contacts, and those infected with HIV. Culture and DST are used for confirmation of MDR TB status for new and Cat I cases that are rifampicin resistant by Xpert MTB/RIF (**Figure. 6**). Laboratory follow-up of DR TB treatment is done by smear microscopy and culture. Second line drugs (SLD) DST is indicated for all positive culture at 4 months of treatment and beyond. Treatment of MDR TB is monitored by microscopy and culture (1 specimen). Culture is also indicated for patients with Xpert MTB/RIF testing repeatedly failed.

A. SITES WITH NO ONSITE GeneXpert INSTRUMENT

Pulmonary TB is diagnosed by smear microscopy at sites where there is no GeneXpert instrument. Two expectorated sputum samples (spot and early morning) will be collected in accordance with NTP recommendations (MOHFW, National Guidelines and operational Manual for the Tuberculosis Control, NTP, 5th edition, 2013.Since sputum samples may be referred for Xpert MTB/RIF testing, the samples must be of good quality. They must also meet the criteria for Xpert MTB/RIF testing: that a sputum sample should contain no particles and be more than 1ml (although 2-4ml is recommended to allow repeat Xpert MTB/RIF testing or referral if needed). If one or both sputum samples are smear positive, the presumptive TB patient will be initiated on first line treatment. Presumptive DR-TB patients will be treated based on the risk of MDR-TB, as follows, in accordance with NTP recommendations (MOHFW, National Guidelines and operational Manual for the Tuberculosis Control, NTP, 5th edition, 2013:

- High MDR-TB risk patients - those with retreatment cases, lost to follow up, relapses, non-converters (smear positive at month five) & MDR-TB contacts - will be treated with the first-line retreatment regimen (2SRHZE/1HRZE/5RHE) The better quality of two samples (smear positive >1ml, good quality [no particles]) from high MDR-TB risk patients will be referred for Xpert MTB/RIF testing, and the treatment will be reviewed based on the result.
- Low MDR-TB risk patients will be treated with the first line regimen (2RHZE/4RH)
- If both sputum samples are negative, presumptive TB & presumptive DR-TB patients will be assessed clinically, and a chest X-ray performed, if available
- If there is a strong clinical or radiological suspicion of TB, patients will be treated for TB with the first line regimen (2RHZE/4RH) One sputum sample (the better of the two samples (smear positive >1ml, good quality [no particles]) from PLHIV, children and high MDR-TB risk patients (retreatment cases, lost to follow up , relapses, non-converters (smear positive at month five) & MDR-TB contacts) will be referred for Xpert MTB/RIF testing. The patient treatment will be reviewed based on the Xpert MTB/RIF test result.
- If there is no clinical or radiological suspicion of TB, diagnoses other than pulmonary TB should be considered.

B. SITES WITH ONSITE GeneXpert INSTRUMENT

Pulmonary TB is diagnosed by the Xpert MTB/RIF test at sites that have onsite access to a GeneXpert instrument. One good quality expectorate sputum sample will be collected in accordance with Xpert MTB/RIF testing criteria and NTP recommendations (MOHFW, National Guidelines and operational Manual for the Tuberculosis Control, NTP 2013) on the spot and sent for Xpert MTB/RIF testing within 24 hours.

Presumptive TB & presumptive DR-TB patients whose results return '*MTB not detected*' by the Xpert MTB/RIF test will receive clinical and radiological follow up. If there is a strong clinical or radiological suspicion of TB, patients will be treated for TB with the first line regimen (2RHZE/4RH). If there is no clinical or radiological suspicion of TB, other diagnoses should be considered.

- Presumptive TB & presumptive DR-TB patients that are '*MTB detected rifampicin susceptible'* will be started on firstline TB treatment (2RHZE/4RH);
- Presumptive TB & presumptive DR-TB patients that are '*MTB detected rifampicin resistant'* will be followed-up based on the risk of MDR-TB:
- High MDR-TB risk patients will be referred to an MDR-TB treatment initiation center and treated with the second line regimen (MOHFW, National Guidelines and operational Manual for the Tuberculosis Control, NTP, 2013). A new sputum sample will then be collected for referral for culture and DST. Patient treatment will be reviewed based on the culture and DST test result.

- Low MDR-TB risk patients will have the Xpert MTB/RIF test repeated on a new sputum sample.
- The test is repeated if the result is 'error', *'invalid'* or '*no result*'.
- Presumptive TB cases & presumptive DR-TB patients that are '*MTB detected rifampicin indeterminate*' will be started on first-line TB treatment (2RHZE/4RH). The Xpert MTB/RIF *test will be repeated*.

C. REPEAT XPERT MTB/RIF TESTING

The Xpert MTB/RIF test is repeated at the same testing facility using freshly collected (new) sputum sample if:

1. The Xpert MTB/RIF test result is '*error*', '*invalid*' or '*no result'*;
2. The Xpert MTB/RIF test result is '*MTB detected rifampicin indeterminate'*;
3. The Xpert MTB/RIF test result is '*MTB detected rifampicin resistant'*, and the patient is considered at low risk of MDR-TB.

If a new sample is requested, the original result is written in the register and the clinical facility is given the returned request form with an explanatory comment and a new sample request from the patient. Follow-up on presumptive TB & presumptive MDR-TB patients is based on the result of the repeat Xpert MTB/RIF test:

- '*MTB not detected'*- the patient will be clinically & radiologically (if available) assessed for TB. If there is a strong resulting suspicion of TB, patients will be treated with the first line regimen (2RHZE/4RH). If there is no clinical or radiological suspicion of TB, other diagnoses should be considered. Clinicians should consider performing another Xpert MTB/RIF test from a new sputum sample.
- '*MTB detected rifampicin resistant'*- the patient will be referred for a complete DST using LPA testing at NTRL and sent to an MDR-TB treatment initiation center for a short regimen or standardized/individual (SOP- NTP Short regimen, 2017) regimen (MOHFW, National Guidelines and operational Manual for the Tuberculosis Control, NTP, 2013);
- '*MTB detected rifampicin susceptible'*- the will be treated with the first line regimen (2RHZE/4RH) and a new sputum sample will be collected for referral for culture and DST. The patient treatment will be reviewed based on the culture and DST test result.

D. MONITORING TREATMENT

The adoption of the Xpert MTB/RIF test does not eliminate the need for conventional TB microscopy, culture and DST. Microscopy or culture, or both, remain necessary for treatment monitoring (MOHFW, National Guidelines and operational Manual for the Tuberculosis Control, NTP, 2013), since the use of DNA detection (e.g. Xpert MTB/RIF test) is not suitable for monitoring treatment.

XPERT MTB/RIF TESTING IN CHILDREN

The MOHFW has determined that Xpert MTB/RIF testing will be implemented as the initial diagnostic test in all presumptive TB and presumptive MDRTB cases in children. Provision for the diagnosis of TB and MDR-TB in children is made in the National TB Diagnostic Algorithm. An additional recommendation that applies to children is the use of the '*Score Chart for Diagnosis of TB in Children'*. The Score Chart is used with a clinical assessment and X-ray (if available) in smears negative or Xpert MTB/RIF test 'MTB not detected' cases. In cases that the child is too young to produce sputum, the use of gastric washings or induced sputum should be considered. Refer to the NTP recommendations for further information on samples, diagnosis and the treatment of TB in children.

XPERT MTB/RIF TESTING AND EPTB

EPTB refers to TB involving organs other than the lungs (*e.g.*, pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones and meninges). Where possible, EPTB should be bacteriologically confirmed. WHO recommends the following policy on the use of Xpert MTB/RIF to diagnose extra-pulmonary TB (EPTB):

- *Cerebrospinal fluid (CSF)*: Xpert MTB/RIF should be used in preference to smear microscopy and culture as the initial diagnostic test for CSF specimens from patients suspected of having TB meningitis. CSF samples must be >0.1ml to be tested by Xpert MTB/RIF;
- *Lymph node and other tissues*: Xpert MTB/RIF may be used as a replacement test for usual practice (including smear microscopy, culture, and/or histopathology) of testing specific non-respiratory specimens (lymph nodes or other tissue) from patients suspected of having EPTB.

These recommendations do not apply to samples of stool, urine or blood, given the lack of data on the utility of Xpert MTB/RIF for these specimens. Clinical facilities with no onsite GeneXpert instrument will refer all EPTB samples to the Xpert sites or TB Referral Laboratories for culture and DST at NTRL.

IMPLEMENTATION PHASES

GeneXpert EXPANSION PLAN

Policy and objectives:

- The NTP commits itself to the phased implementation of GeneXpert instruments to make testing accessible to those in need, in line with the End TB strategy
- The NTP, with support of its partners, commits to equipping 243 sub-district level facilities with GeneXpert instruments by 2018.

The NSP (2018-2022) and National Laboratory TB Strategic Plan (2016-2020) state the intention of having one GeneXpert instrument per district by 2020, with a total of 215 new machines installed (in addition to 51 old machines installed since 2012). They further state that district level placement is to be achieved through the provision of instruments at each district hospital. This plan calls for the rollout to occur in two phases, using GF support:

- Phase 1 (35 sites): 2017
- Phase 2 (180 sites): 2018-2020

ROLES AND RESPONSIBILITIES OF ALL PARTIES

NATIONAL TB CONTROL PROGRAM (NTP)

LABORATORYWORKING GROUP (LWG)

Policy and objectives:

- The NTP will be responsible for setting policy and guidelines for Xpert MTB/RIF implementation and for coordination of all stakeholders;
- The NTP will establish coordinating committees and mechanisms for collaboration among the NTP and other stakeholders at the national, regional, and district levels;
- The NTP will establish the position of Xpert Focal Person to coordinate operational implementation activities in collaboration with all partners.

- Review and appraise implementation of strategic and annual plans for the Xpert MTB/RIF/ ULTRA Xpert test at all levels.
- Receive and appraise periodic technical and financial progress reports.
- Oversee implementation of operational research, monitoring, and evaluation in order to develop sound, evidence-based best practices in TB diagnostics.
- Advise on adoption of new national/international/ global initiatives on TB diagnostics including Xpert MTB/RIF and ULTRA test implementation.
- Participate in national and international initiatives on TB diagnostics, TB activities and Xpert MTB/RIF, ULTRA test implementation.
- Report to the national TB/HIV coordinating committee on the progress of implementing TB activities, including Xpert MTB/RIF, ULTRA testing.

NTP MANAGER

- Make programmatic decisions pertaining to Xpert MTB/RIF and upcoming ULTRA cartridge test implementation according to WHO guidelines and country policies, including decisions regarding GeneXpert instrument placement.
- Delegate a *GeneXpert Focal Person* responsible for coordination of Xpert MTB/RIF test implementation activities at the country level.
- Provide support to the GeneXpert Focal Person.
- Coordinate implementing partners and the TB program, and promote information sharing, including procurement and funding.
- Oversee the GeneXpert instrument handover process.

GENEXPERT FOCAL PERSON

- Liaise with the NTP manager, director of diagnostic services, head of NTRL, LWG, implementing partners, district TB and leprosy coordinators (DC), regarding Xpert MTB/RIF/ULTRA Xpert implementation.
- Advise the NTP manager and implementing partners on the progress of Xpert MTB/RIF implementation as required.
- With the support of the regional GeneXpert Focal Points and partners: collate countrywide quality indicators, undertake remote and onsite troubleshooting, liaise with the manufacturer, and coordinate stock management.
- Organize training for new sites, re-training and onsite training as required in collaboration with, and with support from, partners.
- Supervise the progress implementation and functionality of GX Alert country wide.
- Organize annual meetings to evaluate progress made, and with GeneXpert Focal Persons at all levels (including partners) coordinate supervisory visits.
- Ensure the funding and sustainability of the Xpert Network country wide.

REGIONAL LABORATORY/ COORDINATORS

- Conduct TB bacteriology testing. Submit samples to NTRL for DST (second line drugs), LPA and species identification tests.
- Plan, train, supervise, and carry out regular quality control of GeneXpert testing activities within their zone.
- Participate in supervision of Xpert MTB/RIF testing in the zone, and train testing site workers involved in Xpert MTB/RIF, in collaboration with the DLT
- Undertake remote and onsite troubleshooting, liaise with the GeneXpert Focal Person, and coordinate stock management within the zone.
- Initiate, coordinate, and collaborate in routine testing and operational research of relevant TB control activities.
- Facilitate DCs, District managers, and laboratory technologists (LT) (GeneXpert users) in collating reports regarding unusual errors from district staff, and report to GeneXpert Focal Person.
- Collate and monitor quality indicator data from the testing sites and alert the GeneXpert Focal Points if needed.
- Include GeneXpert oversight in testing site and clinical supervisory visits.
- Provide support to the GeneXpert Focal Person and respond to requests from NTRL.
- Facilitate, as TOT, the training of clinical staff using clinical training program on the use of Xpert MTB/RIF and ULTRA diagnostics, as well as results interpretation.
- Ensure correct and timely treatment for all cases, and that TB numbers are entered into the TB Laboratory Register.
- Immediately report all detected rifampicin resistance to the MDR Focal Person at the NTP.

CIVIL SURGEON

DISTRICT MANAGERS AND / DISTRICT LAB TECHNOLOGIST

PROGRAM ORGANISER

- Troubleshoot GeneXpert-related issues, and relay reports of unusual errors from facility staff to the NTP Xpert focal person.
- Include GeneXpert oversight in testing site and clinical supervisory visits.
- Support the GeneXpert Focal Person, and respond to their requests;
- Ensure correct and timely treatment for all cases, and that TB numbers are entered into the TB Laboratory Register.
- Immediately report all detected rifampicin resistance to the MDR Focal Person at the NTP.
- Manage stock at the district level

GENEXPERT SUPER-USERS

- Under direction from GeneXpert Focal Person, carry out supervisory site visits on a regular basis.
- Provide onsite training.
- Perform facility-level test management and ordering under supervision of the Laboratory Manager.
- Perform daily testing using the GeneXpert instrument, perform regular maintenance and communicate challenges to the District Laboratory Technologist (DLT).
- Immediately report all detected rifampicin resistance to the MDR Focal Person at the NTP.
- Troubleshoot GeneXpert related issues, and report unusual errors to the GeneXpert Focal Points.
- Ensure functionality of GX Alert and collate data for any further intervention to support supply chain management and quality indicators. Report all information captured to the focal Xpert at NTP

CLINICIANS & HEALTH CARE WORKERS

- Diagnose TB & DR-TB presumptive cases in accordance with the National TB diagnostic algorithm.
- Treat TB, and refer MDR-TB cases as directed in the Manual for Management of Tuberculosis.
- Refer rifampicin resistant cases to the MDR-Unit as directed in the TB diagnostic algorithm;
- Record and report monthly quality indicator data to Designated Laboratory Person.

IMPLEMENTING PARTNERS

- Consult with the NTP regarding placement of GeneXpert machines and provide a plan for placement and handover.
- Formalize agreement with the MOHFW and commit to the objectives of the NSP
- Support the NTP in the rollout of Xpert MTB/RIF and in the upcoming introduction of ULTRA cartridge by providing quality indicator data and regular reports on testing site operations.
- Facilitate technical support during the rollout of the GX alert system country wide. Meet regularly with the NTP, share experiences and contribute to improving access to healthcare in Bangladesh.

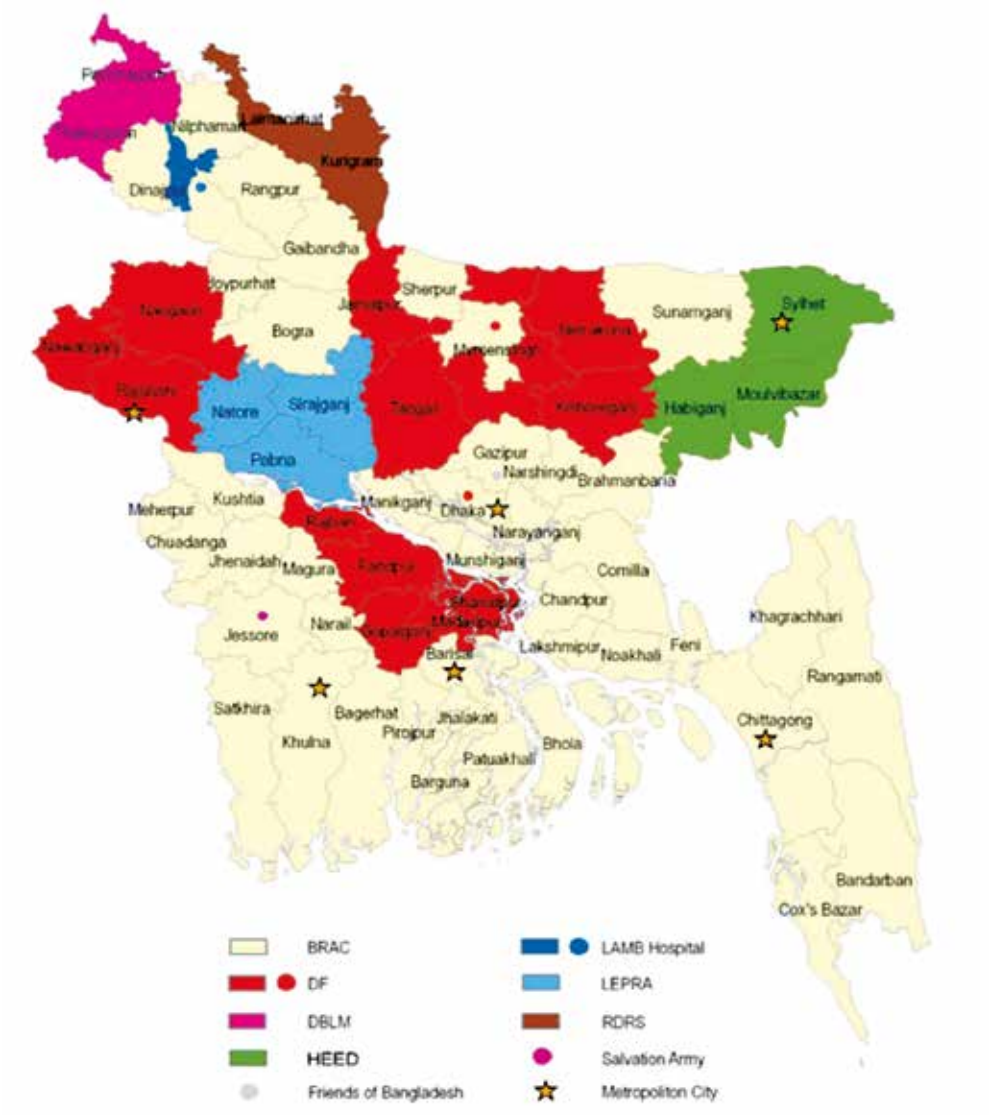
Phased implementation of the Xpert MTB/RIF test requires cooperation and collaboration between the NTP, NTRL and implementing partners.

Within NTP/NTRL, assignment of staff responsible for implementation is necessary to reduce confusion regarding the responsibilities and duties at all levels in Xpert MTB/RIF test implementation. The existing lines of responsibility for the NTP are extended to include Xpert MTB/RIF test operations. All relevant staff should be sensitized regarding their roles and responsibilities.

COORDINATION OF STAKEHOLDERS

The NTP collaborates with approximately fifty national and international health and development agencies to implement the End TB Strategy. To ensure best use of comparative advantages and to avoid fragmentation and duplication of efforts, regular coordination meetings will be held under the Steering Committee for TB. The role of the Steering Committee for TB is to assist in the overall TB program implementation and in the monitoring and evaluation of the NSP. Specific technical working groups have also been set up under NTP to coordinate strategies and activities on PPM and TB/HIV. In addition, a national MDR-TB management coordination committee has been established. Coordination is also ensured through the Country Coordination Mechanism set up for Global Fund collaboration. WHO provides technical assistance to NTP in the area of strengthening national laboratory network, information exchange, improving procurement and supply management, operational research, coordination, collaboration and partnerships, ACSM, and M&E.

Figure 7: Geographical areas of implementation responsibility for key NGOs



BRAC

BRAC is the largest NGO partner of NTP. A Memorandum of Understanding (MoU) was signed between the NTP and BRAC in 1994 for rural areas and in 2001 for urban areas. Along with NTP, since 2004, BRAC is the principal recipient (PR) of GFATM funding for TB in Bangladesh. Under the stewardship of NTP, currently BRAC covers 298 sub-districts (upazillas) of 42 districts with a population of 93 million, including Chittagong hill tracts, 41 prisons, 46 academic institutions, 445 peripheral laboratories, 2 port authority hospitals, 3 EPZ (Chittagong, Karnaphuli, and Comilla) and 11 city corporations. It started its TB control activity in 1984 with its innovative community based approach operated by the Shasthya Shebikas (SS). Shasthya Shebikas plays the pivotal role of connecting individuals with TB control services during household visits and health forums. Each shebikas receives a basic training and a one-day refresher training every month. During household visits, Shasthya Shebikas identify those symptomatic of TB and refer them to the Upazilla Health Complex or BRAC laboratory services for sputum examination. To increase the accessibility of diagnostic facilities, outreach sputum collection centers have been established at the union level (a union is comprised of a few villages). Sputum samples are collected and smeared at the outreach center twice per week. Individuals diagnosed with TB are given Directly Observed Treatment (DOT) by Shasthya Shebikas, usually at their house, under the guidance of the field level staff of BRAC and a government or BRAC medical officer.

Damien Foundation

The Damien Foundation, a Belgian NGO has been active in Bangladesh since 1972. The organization was initially engaged primarily in leprosy elimination in 6 districts. Later on, the organization included Tuberculosis in its agenda, considering the disease burden, and expanded its working area. The organization now covers 14 districts (111 upazillas) of which 13 districts (102 upazillas) are targeted for combined TB and leprosy control. The organization has set up 151 centers including 5 in medical colleges and 1 in workplace (DEPZ). The organization also runs three of its own hospitals with a total 255 beds to guarantee quality services for complicated TB cases (including MDR TB) and leprosy patients. A total of 627 staff nationally, including 11 doctors, are engaged with DF in providing service in Bangladesh. About 25,000 TB cases - including about 200 MDR TB and around 400 new leprosy cases - are being detected and treated by the organization annually. The shortest 9-month Bangladesh regimen for MDR TB, which is being tested now by many other countries, was developed by Damien Foundation Bangladesh.

Other stakeholders include donors (Global Fund, WHO, USAID, icddr,b, Global Drug Facility) and implementing partners (Challenge TB/MSH, IRD, BRAC, Damien foundation, HEED, ICDDR'B, LEPRA, NATAB, PIME Sisters, RDRS, UPHCSDP)

The following guidelines ensure that all stakeholders contributing to Xpert MTB/RIF implementation follow the national guidelines, and that their activities are standardized and coordinated by NTP:

1. All introducing parties (implementing partners and donors) seeking to place a GeneXpert instrument in Bangladesh will hold an initial consultation with the National TB Manager before arranging placement.
2. The introducing party will provide the NTP with a proposal for placement of the GeneXpert instrument(s). The proposal will contain information including:
    a. The duration of the support to be provided by the introducing party. Implementing partners are encouraged to provide a minimum of two years support;
    b. Quantification of the resources being provided by the introducing party regarding reagents, calibration, warranty, maintenance, training (*e.g.* technical / clinical), and technical support;
    c. A transition plan, including how the GeneXpert instrument(s) will be supported after the handover date.
3. The NTP manager, in collaboration with NTRL and the director of diagnostic services and the Xpert focal person, will advise on instrument placement based on the coverage gaps and the strategic objectives of the NTP.

4. The NTP manager, in collaboration with NTRL and Xpert focal person, will consult with the Designated Laboratory Person and/or RTRL Coordinator regarding clinical and testing site readiness, as well as on options for providing continued support beyond the end date of that of the introducing party. Based on the outcomes of these consultations, alternative testing sites may be proposed to the partners or donors. Agreement between NTP and the introducing parties regarding instrument placement will then be reached.

5. A Memorandum of Understanding (MOU) between the MOHFW and introducing parties will be signed. The MOU binds the introducing party to following the NTP guidelines for GeneXpert instrument use, as well as the handing over of a fully functional GeneXpert instrument to the NTP (**Annex: Monitoring Xpert tools**)

6. Following placement of a GeneXpert instrument(s), introducing parties will provide NTP with the following:

    a. Monthly quality indicators reported according to National TB guidelines (see below);

    b. Annual calibration certificates;

    c. Annual progress report outlining testing site activities;

    d. *Ad hoc* reports using the NTP supervision and troubleshooting checklist with additional narrative, if there are any material changes that may affect sustainability of testing after hand-over.

7. Introducing partners shall coordinate the procurement of GeneXpert instruments & reagents with the NTP.

8. NTP shall schedule an annual meeting with the introducing partners to discuss matters of mutual interest.

9. Introducing partners shall advise the NTP of transfer a minimum of six months before the intended handover of the GeneXpert instrument (**see Annex-Monitoring tool - GeneXpert Instrument Handover**).

Xpert PLACEMENT STRATEGY

The Xpert MTB / RIF system is suitable for use at the district and peripheral level, and its allocation should not be limited to the central level or the reference laboratory level. Although testing with this system does not require additional laboratory equipment, advanced equipment does have certain handling requirements i.e.. a stable and uninterrupted power supply to avoid interruption and subsequent loss of results, security against theft, sufficient space for storing cartridges, dedicated testing personnel, and biosafety procedures comparable to those for microscopy.

SELECTION CRITERIA FOR PLACEMENT OF GeneXpert MACHINE

Selection of the districts included in each phase was determined by the TWG experts, approved by the TB Program Manager, and budgeted in the NSP (2018-2022). Determining acceptable sites for GeneXpert instrument placement in Bangladesh involves collaboration between the NTP manager, in collaboration with NTRL, partners, and the GeneXpert Focal Person. Together, they consider epidemiological data on TB, current Xpert machines workload, MTB/RIF testing centers, and Xpert MTB/RIF testing capacity to make the determination. When proposing sites for GeneXpert placement, TWG members are encouraged to prioritize:

- *Clinical and testing sites with high TB, MDRTB and HIV burden priority (i.e. annual TB diagnosis per facility of >500, or cases currently enrolled in HIV chronic care >1000);*
- *Clinical and testing sites in congregate setting (slam area, school, university hospital, prisons,*
- *Urban cities with a high burden of TB, and/or MDRTB according to the prevalence survey findings.*
- *Clinical and testing sites with adequate infrastructure and that are conveniently located for sample referral linkages, site supervision, and data collection activities;*
- *Clinical and testing sites that currently provide care and treatment services for TB and MDR-TB cases.*

GeneXpert TESTING CAPACITY

To determine the acceptable sites for the installation of GeneXpert instruments in Bangladesh, epidemiological data on TB as well as current Xpert MTB / RIF test centers and their ability to perform tests have to be taken into account. The annual test capacity of the 4-module GeneXpert instrument is d 2,11280 **test per year (8 tests/ day x 22 working days x 12 months weeks).**

According to the manufacturer's instructions, the true capacity of the Xpert platform is 12 to 16 tests per day if a facility or hospital is running a 24 hour service.

It is advisable to expand access by developing a strong network and a specimen referral system to increase the demand and the use of all machines, as well as to implement the new algorithm to increase utilization of GeneXpert machines.

CURRENT LOCATION OF EXISTING GeneXpert INSTRUMENTS

Currently Bangladesh has 163 GeneXpert machines operating in the NTP network . The NTP plans to expand its network of Xpert machines to all districts and big hospitals and upazilas.

However, CTB supports 39 machines which are connected to GX Alert, with a plan of expansion to all networks under the GF / NSP plan by 2018.

The strategy to extend the Xpert MTB / RIF test in Bangladesh will be based on the implementation of Xpert technology at additional sites whose location will be guided by the following criteria, additional to those established above:

- Decentralized health care.
- A high burden of MDR-TB or HIV-associated TB.
- Estimated workload of the site (taking into account that the capacity of a four-module GeneXpert unit can be increased from 4 up to 12 tests per workday).
- Sufficient infrastructure, including a stable power supply, secure room(s) for the GeneXpert unit, a computer and cartridges, and adequate room temperature.
- A dedicated staff that can be trained to do the tests and maintain the equipment.
- The ability to provide treatment and follow-up (DOTS) for patients with TB and MDR-TB who are detected at the facility or in the immediate referral sites.

The complete list (at the time of writing) detailing instrument placement, implementing partners, and number of modules per instrument can be found in **Table 4** below.

Since being introduced, GeneXpert instruments (for routine clinical services) have performed a total of 141,399 Xpert MTB/RIF tests; with 49,820 TB positive results and 4097 rifampicin-resistant results being reported to NTP (from starting up to 2016).

Table 4. GeneXpert Machine location (163machines)

No.	Site Name	Location	Model (Number of modules)
1	Sadar Hospital, Barguna	Barguna	GX4
2	Upazila Health Complex, Bakerganj	Barisal	GX4
3	Upazila Health Complex, Lalmohon	Bhola	GX4
4	Sadar Hospital, Jhalakati	Jhalakati	GX4
5	Upazila Health Complex, Bauphal	Patuakhali	GX4
6	Chest disease Clinic (CDC), Pirojpur	Pirojpur	GX4
7	Upazila Health Complex, Nasirnagar	Chittagong	GX4
8	Upazila Health Complex, Hajiganj	Chandpur	GX4
9	Chittagong Medical College Hospital, Chittagong	Chittagong	GX4
10	Comilla Medical College Hospital, Comilla	Comilla	GX4
11	Upazila Health Complex, Debiddwar	Comilla	GX4
12	Upazila Health Complex, Teknaf	Cox's Bazar	GX4
13	Upazila Health Complex Ukhia	Cox's Bazar	GX4
14	Chest disease clinic (CDC), Feni	Feni	GX4
15	Upazila Health Complex, Sonagazi	Feni	GX4
16	Sadar Hospital, Khagrachari	Khagrachari	GX4
17	Sadar Hospital, Lakshmipur	Lakshmipur	GX4
18	Upazila Health Complex, Ramganj	Lakshmipur	GX4

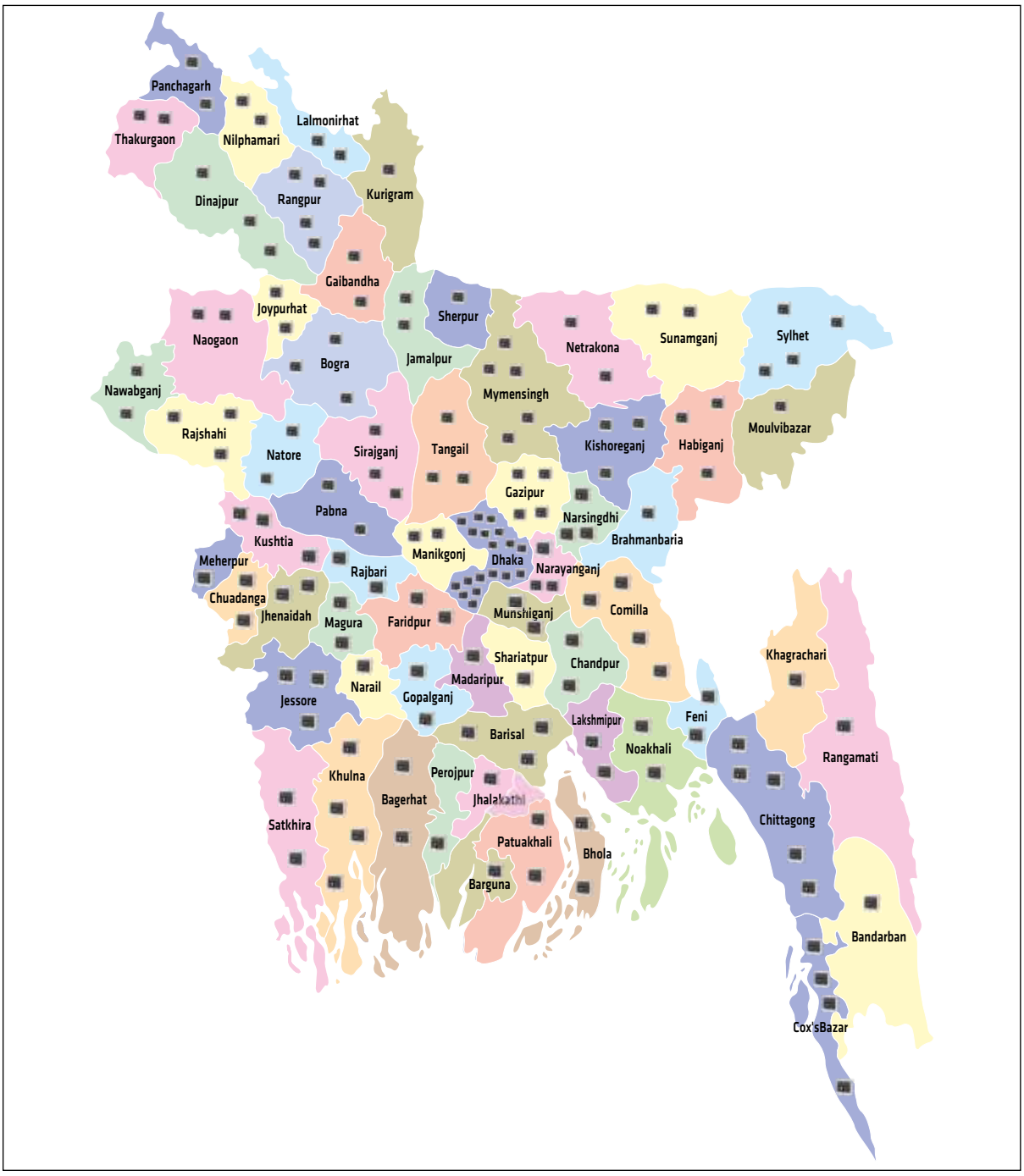
No.	Site Name	Location	Model (Number of modules)
19	National Medical College Hospital, Dhaka	Dhaka	GX4
20	Shaheed Suhrawardy Medical College Hospital, Dhaka.	Dhaka	GX4
21	Faridpur Medical College Hospital, Faridpur	Faridpur	GX4
22	Upazila Health Complex, Kaliakoir	Gazipur	GX4
23	Upazila Health Complex, Tungipara	Gopalganj	GX4
24	Jahurul Islam Medical College Hospital, Bajitpur	Kishoreganj	GX4
25	Upazila Health Complex, Bhairab	Kishoreganj	GX4
26	Sadar Hospital, Madaripur	Madaripur	GX4
27	Upazila Health Complex, Daulatpur	Kushtia	GX4
28	Sadar Hospital, Munshiganj	Munshiganj	GX4
29	Upazila Health Complex, Sirajdikhan	Munshiganj	GX4
30	Upazila Health Complex, Rupganj	Narayanganj	GX4
31	Sadar Hospital, Narsingdi	Narsingdi	GX4
32	Upazila Health Complex, Raipura	Narsingdi	GX4
33	Sadar Hospital, Rajbari	Rajbari	GX4
34	Upazila Health Complex, Pangsha	Rajbari	GX4
35	Sadar Hospital, Shariatpur	Shariatpur	GX4
36	Chest disease clinic (CDC), Tangail	Tangail	GX4
37	Upazila Health Complex, Mirzapur	Tangail	GX4
38	Chest Disease Clinic (CDC), Bagerhat	Bagerhat	GX4
39	Upazila Health Complex, Moralganj	Bagerhat	GX4
40	Upazila Health Complex Alamdanga	Chuadanga	GX4
41	Upazila Health Complex, Monirampur	Jessore	GX4
42	Sadar Hospital, Jhenaidah	Jhenaidah	GX4
43	Upazila Health Complex, Shailkupa	Jhenaidah	GX4
44	Khulna Medical College Hospital, Khulna	Khulna	GX4
45	Upazila Health Complex, Paikgacha	Khulna	GX4
46	Upazila Health Complex, Doulatpur	Kushtia	GX4
47	Chest Disease Clinic (CDC), Magura	Magura	GX4
48	Upazila Health Complex, Shalikha	Magura	GX4
49	Chest Disease Clinic (CDC), Meherpur	Meherpur	GX4
50	Sadar Hospital, Narail	Narail	GX4
51	Upazila Health Complex, Shyamnagar	Satkhira	GX4
52	Chest Disease Clinic (CDC), Jamalpur	Jamalpur	GX4
53	Upazila Health Complex, Islampur	Jamalpur	GX4
54	Upazila Health Complex, Bhaluka	Mymensingh	GX4

No.	Site Name	Location	Model (Number of modules)
55	Upazila Health Complex, Durgapur	Netrokona	GX4
56	Sadar Hospital, Sherpur	Sherpur	GX4
57	Upazila Health Complex, Sreebordi	Mymensingh	GX4
58	Upazila Health Complex, Dupchanchia	Bogra	GX4
59	Joypurhat District Modern Hospital	Joypurhat	GX4
60	Upazila Health Complex, Akkelpur	Joypurhat	GX4
61	Sadar Hospital, Naogaon	Naogaon	GX4
62	Upazila Health Complex, Patnitala	Naogaon	GX4
63	Upazila Health Complex, Baraigram	Natore	GX4
64	Chest Disease Clinic (CDC), Chapai Nawabganj	Chapai Nawabganj	GX4
65	Upazila Health Complex, Gomostapur	Chapai Nawabganj	GX4
66	Upazila Health Complex, Chatmohor	Pabna	GX4
67	Rajshahi Medical College Hospital, Rajshahi	Rajshahi	GX4
68	Upazila Health Complex, Belkuchi	Sirajganj	GX4
69	Chest Disease Clinic (CDC), Dinajpur	Dinajpur	GX4
70	Upazila Health Complex, Birampur	Dinajpur	GX4
71	Upazila Health Complex, Palashbari	Gaibandha	GX4
72	Upazila Health Complex, Nageswari	Rangpur	GX4
73	Sadar Hospital, Lalmonirhat	Lalmonirhat	GX4
74	Upazila Health Complex, Hatibandha	Lalmonirhat	GX4
75	Sadar Hospital, Nilphamari	Nilphamari	GX4
76	Upazila Health Complex, Dimla	Nilphamari	GX4
77	Sadar Hospital, Panchagarh	Panchagarh	GX4
78	Upazila Health Complex,Tetulia	Panchagarh	GX4
79	Rangpur Medical College Hospital, Rangpur	Rangpur	GX4
80	Upazila Health Complex, Ranisankoil	Thakurgaon	GX4
81	Upazila Health Complex, Chunarughat	Habiganj	GX4
82	Sadar Hospital, Moulvibazar	Moulvibazar	GX4
83	Upazila Health Complex, Chhatak	Sunamganj	GX4
84	Sylhet MAG Osmani Medical College Hospital	Sylhet	GX4
85	Upazila Health Complex, Beanibazar	Sylhet	GX4
86	NTRL-1	Dhaka	GX16
87	NTRL-2	Dhaka	GX16
88	NTRL-3	Dhaka	GX16
89	NTRL-4	Dhaka	GX16
90	CDC Shamoli	Dhaka	GX16

No.	Site Name	Location	Model (Number of modules)
91	BIRDEM Hospital	Dhaka	GX16
92	BSMMU Hospital	Dhaka	GX16
93	RTRL-Chittagong	Chittagong	GX16
94	CDH Pabna	Pabna	GX4
95	CDC Khulna	Khulna	GX4
96	CDC Jessore	Jessore	GX4
97	CDC Kushtia	Kushtia	GX4
98	CDC Gaibandha	Gaibandha	GX4
99	CDC Satkhira	Satkhira	GX4
100	CDC Kurigram	Kurigram	GX4
101	CDC Chuadanga	Chuadanga	GX4
102	CDC Barisal	Barisal	GX4
103	CDC Bhola	Bhola	GX4
104	CDC Gopalgonj	Gopalganj	GX4
105	CDH Faridpur	Faridpur	GX4
106	CDC Chandpur	Chandpur	GX4
107	CDC Comilla	Comilla	GX4
108	CDC Noakhali	Noakhali	GX4
109	CDH Sylhet	Sylhet	GX4
110	CDC Sunamgonj	Sunamganj	GX4
111	UHC Sreemongal	Sreemongal	GX4
112	CDC Bogra	Bogra	GX4
113	CDC Patuakhali	Patuakhali	GX4
114	CDC Cox'sbazar	Cox's Bazar	GX4
115	CDC Rangamati	Rangamati	GX4
116	RTRL-Rajshahi	Rajshahi	GX4
117	CDC B.Baria	B.Baria	GX4
118	CDC Rangpur	Rangpur	GX4
119	Netrokona TB Hospital	Netrokona	GX4
120	DF Hospital Mymensingh	Mymensingh	GX4
121	Jalchatra Hospital-Tangail	Tangail	GX4
122	Gazipur Sadar Hospital	Gazipur	GX4
123	CDC Kishorgonj	Kishoreganj	GX4
124	CDC Thakurgaon	Thakurgaon	GX4
125	Bandarban Sadar Hospital	Bandaban	GX4
126	Chankarpol	Dhaka	GX4

No.	Site Name	Location	Model (Number of modules)
127	BITD, CTG	Chittagong	GX4
128	AF Patho Inst	Dhaka	GX4
129	Gen/M C Hosp Sirajgonj	Sirajganj	GX4
130	Sadar Hosp Habiganj	Habiganj	GX4
131	Capt.M.Ali MCH	Dhaka	GX4
132	DMCH	Dhaka	GX4
133	Med C Hosp, Manikgong	Manikgong	GX4
134	Sadar Hosp,Narayangong	Narayanganj	GX4
135	Med Colege Hosp, Mymensingh	Mymensingh	GX4
136	CDC Natore	Natore	GX4
137	Gen/M C Hosp Sirajgonj	Sirajganj	GX4
163	Rampura TBSTC	Dhaka	GX4
139	TB Diagnostic Center , BRAC, Barisal	Barisal	GX4
140	TB Diagnostic Center , BRAC, Khulna	Khulna	GX4
141	TB Diagnostic Center , BRAC, Rajshahi	Rajshahi	GX4
142	TB Diagnostic Center , BRAC, Rangpur	Rangpur	GX4
143	TB Diagnostic Center , BRAC, Gazipur	Gazipur	GX4
144	TB Diagnostic Center , BRAC, Comilla	Comilla	GX4
145	TB Diagnostic Center , BRAC, Dinajpur	Dinajpur	GX4
146	TB Diagnostic Center , BRAC, Bogra	Bogra	GX4
147	TB Diagnostic Center , BRAC, Savar,Dhaka	Dhaka	GX4
148	TB Diagnostic Center , BRAC, Keranigonj,Dhaka	Dhaka	GX4
149	TB Diagnostic Center , BRAC, Manikgonj	Manikgong	GX4
150	TB Diagnostic Center , BRAC, Narsingdi	Narsingdi	GX4
151	TB Diagnostic Center , BRAC, Noakhali	Noakhali	GX4
152	TB Diagnostic Center , BRAC, Cox's Bazar	Cox's Bazar	GX4
153	TB Diagnostic Center , BRAC, Jessore	Jessore	GX4
154	TB Diagnostic Center , BRAC, Narayangonj	Narayanganj	GX4
155	TB Diagnostic Center , BRAC, Mymensingh	Mymensingh	GX4
156	TB Diagnostic Center , BRAC, Matuail, Dhaka	Dhaka	GX4
157	TB Diagnostic Center , BRAC, Bakulia, Chittagong	Chittagong	GX4
158	TB Diagnostic Center , BRAC, Tongi, Gazipur	Gazipur	GX4
159	TB Diagnostic Center , BRAC, Mirpur-1, Dhaka	Dhaka	GX4
160	TB Diagnostic Center , BRAC, Sylhet	Sylhet	GX4
161	TB Diagnostic Center , BRAC, Badda, Dhaka	Dhaka	GX4
162	Sir Salimullah Medical College	Dhaka	GX4
163	Sadar Hospital Habiganj	Habiganj	GX4

Figure 8. below is the Bangladesh administrative map with the first 163 GeneXpert machine placements from 2014 to 2017.



Plan of Cartridges needs from 2018 to 2022 according to the NSP PLAN (2018-2022)

Table 5, below, shows the 5-year forecast plan for all 615 new machines and 163 + 30 operated by ICDDR,B total 193 existing machines expected to run from 2018 to 2022. The capacity of each machine is calculated as 2112 tests per year, taking into account that 75% of modules are functional at a time. So if 2 cycles per day are run on each of the 4 modules of each of the 243 Xperts, and there are 22 working days in a month, then 449,856 cartridges are required (because 243x8x22x12= 513,216).

As maximum 75% modules were functioning then 513,216x75%=384,912 cartridges with the new algorithm introduction for all TB suspect cases in line with the universal DST access which will also boost the use of machines.

Table 5. Five year forecast for new and existing GeneXpert machines

Year	Number of instruments	Number of cartridges	Test cost including cartridges and consumables (per test 16.207)
2017	193 existing network	**305,712**	**4,954,674**
2018	243	384,912	4,954,674
2019	243	384,912	6, 238,269
2020	296	468,864	7, 598,878
2021	496	785,664	12,733,256
2022	615	974,160	15,788,211

***2017:** Cartridges already purchased by CTB and NTP through GF.

BUDGET AND RESOURCE MAPPING

According to the NSP 2018-2022 of the NTP, a total of 615 GeneXpert instruments are to be installed in Bangladesh by 2022. However funds have been secured 213 machines to achieve planned expansion by June 2020.

Table 6. New GeneXpert MTB / RIF machines in Bangladesh according to the NSP (2018-2022)

Item	2018	2019	2020	2021	2022
Procurement and Installation of new GeneXpert instruments	50	0	53	200	119

To provide the cost of implementing and maintaining Xpert MTB/RIF test rollout in Bangladesh, a five-year cost mapping exercise was conducted using the following assumptions:

1. Currently, there are 193 GeneXpert instruments in Bangladesh. The goal is to achieve a total of 615 machines by 2022.
2. There will be a total of 296 GeneXpert instruments by June 2020, including the original 51. The capital costs associated with procuring the remaining 215 are calculated in Table 7. A total of 319 more machines are planned between 2021 and 2022, pending approval from GF.

Table 7. Capital costs associated with procurement of 215 GeneXpert machines

Item/ Fiscal Year	2017	2018	2019	2020	2021	2022
Number of sites/Instruments	142	50	0	53	200	119
GeneXpert instrument (GX4)	US$17,500	US$17,500	N/A	US$17,500	US$17,500	US$17,500
Shipping cost	US$ 7,000	US$ 7,000	N/A	US$ 7,000	US$ 7,000	US$ 7,000
Uninterrupted power supply	US$ 1,250	US$ 1,250	N/A	US$ 1,250	US$ 1,250	US$ 1,250
TOTAL (US $)	**3,656,500**	**1,287,500**	**0**	**1,364,750**	**5, 150,000**	**3,064,250**

3. **Installation costs** associated with instrument placement are shown in Table 8. These costs are estimated based on a pre-installation site assessment (equivalent to one supervisory visit) and a site upgrade, priced in US$ per site (*e.g.* installation of air conditioner, upgrade to benches, upgrade to testing site security). Follow-up site visits (equivalent to one supervisory visit) were budgeted to take place at 15% of testing sites. In addition, all new testing sites receive a comprehensive assessment within three months of installation, equivalent to a two day supervisory visit.

Table 8. Installation costs associated with GeneXpert placement and installation (US $)

Activity	2017	2018	2019	2020	2021	2022
Upgrade costs per site	8,200	8,200	0	8,500	8,500	8,500
Pre-Installation assessment	315	330		350	350	350
Comprehensive assessment	420	440		450	480	480
Follow-up assessment and number of visit	315 x 2	320x2		350x2	350x2	350x2
Number of Instrument/ sites	142	50		53	200	119
TOTAL	**1,358,230**	**480,500**	**0**	**530,000**	**20,06,000**	**1,193,570**

4. **The training costs** (shown in Table 9) are estimated based on one three-day training for 12 new users as a batch using the new training package developed by the NTP based on the GLI training module, and in collaboration with Cepheid. To accommodate the trainings of new users associated with operation and maintenance, trainings are proposed for 2017 through 2020. In addition, refresher on-site training will be conducted for existing sites every year according to need and weakness observed during supervision.

Table 9. Training costs

	2017	2018	2019	2020	2021	2022
Total personnel need to be trained (+refresh training for new staff)	114	156	0	108	250	150
Total batch	19	13	0	9	21	13
Unit cost per batch	2150	2150	0	2300	2400	2500
TOTAL (US $)	**40,850**	**27,950**	**0**	**20,700**	50,400	**32,500**

5. **Supervisory visits.** The costs of one-day and two-day supervisory visits are shown below. Site supervision visits are scheduled as outlined in the implementation plan:

- New sites, and existing sites performing optimally, will receive four one day (quarterly) supervisory visits per annum;
- The 30% of existing sites judged to be performing sub-optimally, will receive one-day (quarterly) supervisory visits per annum and optional one additional day for corrective action /refresh training when needed.

Table 10. Supervisory visit unit costs (US $)

	One day	Two days
Travel/ Per diem	75	150
Hotel Accommodation	35	75
Stationary	10	10
Contingency	25	50
TOTAL	**145**	**285**

Table 11. Supervisory visit costs (US $)

	2017*	2018	2019	2020	2021	2022
New sites supervision	0	50 x (4x 145)	0 x (4x145)	53 x (4x145)	200x(4x145)	119x(4x145)
Sub total	**0**	**29,000**	**0**	**30,740**	**116,000**	**69,020**
Existing sites supervision (optimal)	51x (4x145)	193 x (4 x 285)	243 x (4 x 285)	243 x (4 x 285	296 x (4x 285)	496 x (4x285)
Sub total	**29580**	**220,020**	**277,020**	**277,020**	**337,440**	**565,440**
Existing sites Sub optimal (corrective action needed)	0	12 x(1 x 285)	20 x (1 x 285)	15x (1 x285)	20x (1x285)	20x (1x285)
Sub total	**0**	**3420**	**5700**	**4275**	**5700**	**5700**
TOTAL	**29580**	**252,440**	**282,720**	**312,035**	**459,140**	**640,160**

2017*: Already budgeted by CTB and NTP in the current GF Round and ongoing activities.

6. Consumables

The estimated costs of consumables are shown below and in Tables 12 and 13:

- One calibration kit is used per instrument per year;
- The annual test capacity of the 4-module GeneXpert instrument is 1040 test per year (4 tests/day x 5 working day x 52 weeks) using the current algorithm (2016).
- It is estimated that with a good transport system in place and new algorithm to be developed in 2018, the site will increase and run eight tests per day (1500 tests) will be performed per instrument from year two, taking in account 75 % capacity.

Table 12. Consumables and Running cost

Variable costs	Unit price in US$
Shipment cost per cartridge	1.40
Alcohol 70%	0.05
Concentrated bleach	0.007
Tissue	0.79
Falcon tube	0.15
Gloves	0.83
Other costs (e.g. Sample referral)	3
Sub total	**6.227**
Cost per cartridge	9.98
TOTAL per test	**16.207**

7. Warranty & maintenance

Two options are available under the CEPHEID contract with a country:

Option 1: Purchase of three-year extended warranty at US$ 7902 per instrument (This is the preferred option).

Option 2: Module replacement at a cost of US$ 3,360 per module

* In 2015/16 (60 modules of 39 instruments) were replaced. Analysis of this data shows that it is more cost-effective to purchase the extended warranty, so Bangladesh follows the warranty procurement process.

Table 14. Warranty and Maintenance cost

	2017	2018	2019	2020	2021	2022
Total number of modules	300	868	1068	1280	2080	2556
Total new machines procured	**142**	**50**	**0**	**53**	**200**	**119**
Projected number of existing instruments failing calibration (estimated at 10% - 20%)	4-8	5-10	6-12	7-14	8-16	8-16
Module Replacement cost (3 Year warranty cost for new procured machines which will cover any failed module replacement for a period of 5 years	US$ 1,122, 048	396,000	0	418,806=	1, 580,400	940,338
TOTAL						

: The standard warranty is two years, starting from the date of invoice, so a 3 year warranty extension covers the instrument for 5 years from date of invoice. If after this period the machine is still under the NTP program, they can procure a one year extension contract at the cost of US$2,898, or a an additional three year warranty coverage at the cost of US$7,902.

8. Remote connectivity

GX Alert connects GeneXpert machines to the internet and allows all devices to be managed and monitored from a distance in order to improve maintenance and coordination. The system also provides patients fast feedback on their results, referring clinicians and treatment centers, which in turn will improve TB treatment. GX Alert remote monitoring system was introduced in Bangladesh in 2015 by the USAID-funded Challenge TB Project under MSH. Table 15 shows the costs associated with maintenance and support of the GX network coverage up to 2019 for 39 machines.

Table 15a. GX Alert running costs (US$) as supported by CTB from 2016-2019 for 39 sites

Activities/ Item	2016	2017	2018	2019
Preparation & Mobile connectivity	35,816	3,295	3,295	3,295
In-country training	18,110	0	0	0
Rapid roll out & Maintenance of the GX Alert system	26,710	28,980	15,260	8,890
Follow-up deep dive data training	0	15,210	6,832	6,932
Other direct costs (ODC)	6,897	2,309	6,509	2,309
One-time expenses	8,180	0	0	0
Total per year (US $)	95,712	49,793	31,895	21,425

Table 15b. GX Alert running of new procured machines under GF support (2018-2022)

Activities/ Item	2017	2018	2019	2020	2021	2022
Number of New GeneXperts	**184 4 (including iccdrb machines)**	**50**	**0**	**53**	**200**	**119**
All inclusive cost with five warranty for GxAlert expansion per GeneXpert machine 5500USD)	847, 000	275,000	39 (as CTB support will end in 2018)	291,500	1,100,000	654, 500
Total per year (US$)	**1,012, 000**	**275,000**	**214,500**	**291,500**	**1,100,000**	**654, 500**

9. Program evaluation

The estimated cost associated with the biannual partners meetings to evaluate Xpert MTB/RIF rollout and program implementation is shown in Table 16.

Table 16. Program evaluation cost (US $)

	40 participating staff
Travel	300
Periderm	2,200
Conference room	1,400
Stationary	200
Contingency	450
TOTAL (US $)	4,550

Other budgetary considerations

- Additional annual human resource costs are to be estimated by the NTP.
- The NTP aims to increase the proportion of optimal performing sites to more than 90% by the end of 2018. Trouble shooting and re-training will play an important part in meeting this goal. Reducing the percentage of suboptimal sites will reduce the yearly costs related to future support.
- It is more cost effective to increase testing at fewer sites than to install additional instruments; therefore, the program aims to utilize maximum capacity of instruments, or approximately 12 tests per day or 240 tests per month. To achieve this, the location of current instruments may be reassessed to ensure optimal placement. Patient referral from sites within the district will be encouraged and systems strengthened.

- To determine resource gaps, implementing partners will submit detailed budgets related to Xpert roll out to the NTP, and commit to at least two years of support following GeneXpert placement. In-country implementing partners will also provide annual estimates of costs, and describe what is covered by the budget, as well as the funding gaps. It is most important to provide a date for handover and to work with the NTP in the months before handover to allow a smooth transition, including budgeting for sites.
- Cost effective implementation requires testing and harmonization of clinical sites. For budgeting purposes, activities will be combined to reduce costs. For example, clinical preinstallation assessments will be conducted at the same time as testing site readiness assessments, either by the same person or with an additional clinically trained and authorized person.
- The number of diagnosed MDR-TB cases will increase due to the Xpert MTB/RIF test and roll out. Additional costs to be considered resulting from this include
    - Transport of cases to Treatment Initiation Centers
    - Food and housing at a TB hospital
    - Cost of culture to confirm and monitor treatment program
    - Treatment costs

AVAILABLE RESOURCES

The NTP estimated that in 2018, US $56,942,582 was required to fund the Bangladesh TB program under the NSP (2018-2022).

However, 34% of the program remains unfunded. This presents challenges when attempting to achieve the goal of placing one instrument per district, per the *National TB Laboratory Strategic Plan*, given the significant expenditure required versus resources available. Sustained efforts are required to mobilize resources to ensure uninterrupted operation of existing GeneXpert instruments, and to sustainably finance full district-level coverage. Coordinating and adequately mapping incoming resources associated with GeneXpert as per the previous sections (**Budget and Resource mapping**) will allow sufficient time to incorporate ongoing costs into the planning cycles of appropriate funding mechanisms. A monitoring system will be established at the NTP to assist with this function.

FUNDING SOURCES

Since the Bangladesh MOHFW decided to adopt the WHO recommendations for the use of Xpert MTB/RIF in the diagnosis of HIV-associated TB and MDR-TB, the country has been the recipient of significant international support for its introduction. The following major global mechanisms have supported Xpert roll out:

Global Fund to Fight AIDS, Tuberculosis and Malaria*:* The Global Fund will continue to be a critical source of support for GeneXpert rollout in Bangladesh. Costs for one year of operations were included in the interim Global Fund proposal submitted in early 2014. It is imperative that Global Fund concept notes and proposal submissions developed in 2017 include financing for GeneXpert rollout and include this implementation plan and budget in the NSP (2018-2020), taking into consideration the interim proposal grant awarded and other commitments. As future concept notes must be developed in collaboration with the National AIDS Program, joint budgeting and planning regarding GeneXpert will be required between the two programs.

Domestic funding: Increases in domestic funding allocations are required to ensure the sustained use of GeneXpert beyond the life of the various projects currently operating. A key step will be the inclusion of ongoing running costs and commodities for the instruments into comprehensive health plans by the NTP and MOHFW. It is advised that a minimum of supervision and other system costs are included in the regional health management team and medium-term development budgetary submissions. Ownership of GeneXpert instruments by facilities and district authorities is important to ensure sustained use. This is why it is essential to involve the district and relevant facility authorities in the initial phases, and for close linkages to be formed between the NTP and the Department of Diagnostic Services. Increasing domestic funding for the TB program in general was highlighted as a key area for action by the MOHFW in its own master plan. It is critical that funding for GeneXpert and other diagnostic technologies play a central role in those ongoing discussions.

***Other bilateral and multilateral donors**:* These donors (i.e. USAID, GFATM, etc.) currently provide resources for GeneXpert instruments and activities in Bangladesh. As these donors plan the next iterations of their support, it will be important for them to work with the NTP early in the planning process to ensure that future projects are aligned to address coverage gaps, and strive to supplement the resources committed as captured by ongoing resource mapping. Evaluation of NTP data from GxAlert tool and related implementing partners' reports from ongoing implementation will be critical to informing roll out and financing plans.

Implementing Partners: The NTP collaborates with a number of national and international health and development agencies to implement the End TB Strategy. To ensure best use of comparative advantages, and to avoid fragmentation and duplication of efforts, regular coordination meetings are held under the NGO Steering Committee for TB. The role of the Steering Committee for TB is to assist the overall TB program implementation and monitoring and evaluation of the national strategic plan. Specific technical working groups have also been set up under NTP to coordinate strategies and activities on PPM and TB/HIV. In addition, a national MDR-TB management coordination committee has been established. Coordination is also ensured through the Country Coordination Mechanism set up for Global Fund collaboration. WHO provide technical assistance to NTP in the area of strengthening national laboratory network, capacity building, information exchange, resource mobilization, regular supplies of drugs and improving procurement and supply management, operational research, collaboration and partnerships, ACSM, monitoring and evaluation.

Table 17. Funds available for support from donor agencies and implementing partners (US $)

	2017	2018	2019	2020	2021*	2022*
GF	2,102,000	3,969,000	1,736,000	4,706,000	5,448,000	15,010,000
CTB	117, 000	0	0	0	0	
TOTAL	2,219,000	3,969,000	1,736,000	4,706,000	5,448,000	15,010,000

*: Budget expected but not yet funded (Gap)

XPERT MTB/RIF TEST ROLLOUT COSTING

To provide the cost of implementing and maintaining Xpert MTB/RIF test rollout in Bangladesh, a five- year cost mapping exercise was conducted during the validation workshop held in Dhaka on 25 to 27 April which will be included in the NSP plan (2018-2022) (**Table 18**).

Table 18. Five-year cost mapping Xpert MTB/RIF implementation plan in Bangladesh (2018-2022) in US $

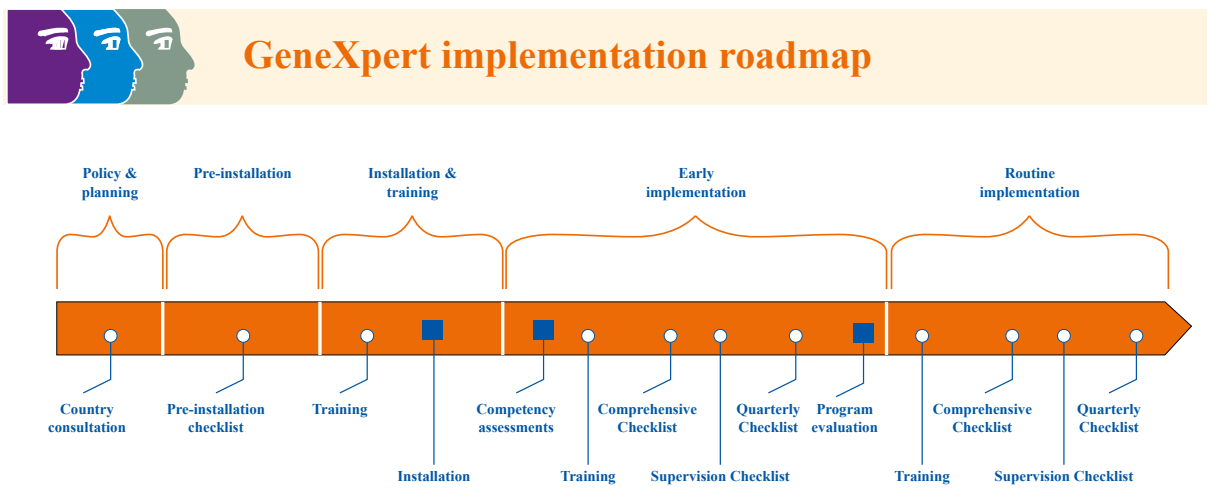
Fiscal Year	2017	2018	2019	2020	2021*	2022*
Number of GeneXpert instruments	51+142 New	193+50 New	243	243+53 New	296 +200 New	496+119 New
Capital	**3,656,500**	1,287.500	0	1,364.750	5,150,000	**3,064,250**
Refurbishment of sites and Installation of new machines	**1,358,230**	**480,500**	0	**530,000**	**20,06,000**	**1,193,570**
Training	40,850	27,950	0	20,700	50,400	**32,500**
Supervision	22,620	**252,440**	**282,720**	**312,035**	**459,140**	**640,160**
Consumables	**4,954,674**	6, 238,269	7, 598,878	12,733,256	12,733,256	15,788,211
Warranty & Maintenance	US$1,122, 048	396,000	0	418,806	1, 580,400	940,338
GX Alert (connectivity)	1,012, 000	275,000	**214,500**	291,500	1,100,000	654, 500
Program evaluation	4,550	4,550	4,550	4,550	4,550	4,550
Total implementation plan/year	**10,037,424**	**5,345,970.60 1,437,727.50**	**4,390,682.00 501,770**	**7,887,442.00 14,312,211.75**	**13,689,143.00 14,927,746**	**18,551,243.00 21,663,579**

*: Budget to be completed at the time of next negotiation with GF as agree by NTP as still a GAP to be mobilized.

IMPLEMENTATION ROADMAP

As Bangladesh scales up the use of the Xpert MTB/RIF test for case detection, there is an urgent need for standardized processes and tools to assist in better M&E for Xpert MTB/RIF test implementation. The NTP has implemented a standardized comprehensive M&E framework that includes all programmatic and testing site aspects of Xpert MTB/RIF test implementation. The M&E framework, represented diagrammatically in **Figure 9**, adopts a phased approach; from site selection and readiness, installation of equipment, training and competency assessment, site monitoring visits, through to handover of GeneXpert instruments from partners/donors to the NTP.

Figure 9: Bangladesh Roadmap to Xpert MTB/RIF Implementation



The roadmap represents implementation at national and site level, though it should be noted that:

- Implementation of the Xpert MTB/RIF test can be considered one of the five rollout phases
- Individual testing sites may vary in their stage of implementation - as some sites implement routine testing, others may be receiving assessment for suitability of instrument placement.
- The role of implementing partners in Xpert MTB/RIF test implementation is crucial. Making use of the M&E framework ensures that implementation roles are clearly identified and that NTP has the key coordinating role and can plan for the capacity to sustain implementation after GeneXpert instrument handover from partners.
- Some operational activities are synchronous and can be initiated in different phases, or may extend beyond *'phase completion'*. The M&E framework is therefore only a guide to implementation and may be customized depending on local circumstances.
- While there is significant emphasis on the implementation of the Xpert MTB/RIF test at the laboratory, implementation also includes initiation of clinical sites.

PHASE 1: POLICY & PLANNING

The implementation of the Xpert MTB/RIF test is led by the NTP and is facilitated by cooperation between the NTP/NTRL, TWG and implementing partners. In-country coordination is essential to optimize the use of resources, streamline activities, and ensure that sound technical advice is delivered and appropriate approaches are used. It is also fundamental to ensure that there is collaboration among the national TB and HIV/AIDS programs, public or private laboratory services, and research institutions investing in TB control.

Policy and objectives:

- The NTP will work with partners from all relevant sectors in planning, implementing, monitoring, and evaluating TB activities to ensure the most effective response to the TB epidemic;
- The NTP will organize and guide utilization of multi-sectorial and multidisciplinary expertise to structure, finance, deliver, and manage TB control activities;
- The NTP will work closely with other departments within MOHFW and other government agencies to further the objectives of the National TB Laboratory Strategic Plan;
- The NTP will coordinate placement of GeneXpert instruments at appropriate locations to meet the objectives of providing TB diagnostic services to all presumptive TB cases;
- The NTP will implement a referral system to provide access to Xpert MTB/RIF testing in remote regions of Bangladesh.

It is essential that the implementation of the Xpert MTB/RIF test be coordinated at the country level. Technical agencies and donors need to work within the framework of the NTP and National AIDS Control Program to assist in implementing Xpert MTB/RIF testing. An increase in the number of cases of TB and MDR-TB detected will require an increase in the capacity for patient management and provision of anti-TB drugs, whether they are PLWHIV patients or children. It is necessary to ensure that cases of MDR-TB are accurately reported and forecast in order to guarantee an uninterrupted supply of quality assured treatment. In addition, sustained and prolonged technical assistance is required to rapidly increase the capacity to deliver care for MDR-TB cases.

PHASE 2: PRE-INSTALLATION

Policy and objectives:

- The NTP will ensure that all sites meet minimum required criteria, including infrastructure, uninterrupted power, and personnel prior to installation of GeneXpert instruments, in order to enable their effective and safe operation.

The pre-installation phase initiates the operational process for Xpert MTB/RIF test implementation. Standardized checklists developed in line with this plan will be used to assess whether testing and clinical sites are prepared for GeneXpert instrument installation (**Annexes**). It is the responsibility of the GeneXpert Focal Person to arrange, conduct and report the outcomes from the preinstallation assessments to the NTP. The GeneXpert Focal Person coordinates the site assessments with the Designated Laboratory Person. The Designated Laboratory Person/RTRL Coordinator will contact the clinical site managers, schedule the visit and make the necessary arrangements for transport and accommodation.

PRE-INSTALLATION SITE VISIT AND CHECKLIST

Clinical site assessments are performed by the lab and M&E Focal persons of NTP, implementing partner technical advisor and/or RTRL Coordinator using standardized checklists (**Annexes**).

Pre-installation clinical site assessments will be performed at least three months before the projected installation date. Clinical site assessment can be logistically challenging due to the number of clinical sites that need to be assessed. The clinical checklist can be used to assess preparedness for Xpert MTB/RIF implementation, and should determine awareness of implementation, potential staff training needs, as well as the capacity to treat TB and refer MDR-TB cases. Testing site (laboratory) assessments can also be performed by the GeneXpert Focal Person and/or the implementing partner technical advisor and/or GeneXpert Focal Points using standardized checklists (**Annex 1 and 2**). Pre-installation testing site assessments will be performed at least three months before the projected installation date. The Testing Site Pre-Installation Checklist assesses preparedness for Xpert MTB/RIF implementation, and should determine whether there is adequate infrastructure and systems to support GeneXpert instrument placement, and identify potential staff for

training (**Annex 1 and 2**). The data gathered by completion of the Pre-Installation Checklist will be used to update the Xpert MTB/RIF Tracking Tool (*see Monitoring & Evaluation*). Testing sites that meet the prerequisite criteria may move to the installation phase. Sites that do not meet the prerequisite criteria may require support to meet these standards. When reporting the outcomes of the pre-installation assessments to the NTP, the implementing partner technical advisor, RTRL Coordinator and/or the GeneXpert Focal Person must provide a brief narrative report along with details of the work required to make upgrades. The NTP and implementing partner will agree on who is responsible for upgrading the facility, and the timeframe for the upgrade. The GeneXpert Focal Person will delegate responsibility for overseeing the upgrading of facilities to the RTRL Cordinator or Laboratory Manager. The Focal Person may arrange a followup visit when the work is complete, or may delegate this responsibility to the RTRL Cordinator. A written confirmation that the upgrade has been completed must be received prior to GeneXpert instrument installation. Each facility that did not meet the pre-requisite standard must be re-assessed for readiness prior to installation. The GeneXpert instruments may be relocated to another testing site if the installation criteria cannot be met.

PHASE 3: INSTALLATION AND TRAINING

Policy and objectives:

- The NTP, in coordination with implementing partners, will train a cadre of testing site users and clinical staff for Xpert MTB/RIF implementation;
- The NTP will designate appropriate staff to act as supervisors (RTRL Cordinator) and GeneXpert Focal Points, whose responsibility it is to provide supervision and technical support to testing sites;
- The NTP aims to have 2 trained, certified users per site and at least one trained focal point per region;
- The NTP will train all RTRL Coordinator on Xpert MTB/RIF testing using standard program by the end of 2018.

The installation phase begins with the delivery of the instruments to the testing sites. Installation of GeneXpert instruments can be performed by trained individuals (GeneXpert Focal Points) or by implementing partners if they have been pre-approved to perform installations by the NTP and CEPHEID and are willing to follow NTP guidelines for installation. The installation dates must be coordinated between the NTP, implementing partners, and the testing sites. To facilitate scheduling, implementing partners will provide at least three months' notice to the NTP as regards proposed installation dates. Installation dates must take into account that GeneXpert instruments can be delayed at customs. The GeneXpert Focal Person or the implementing partner will finalize installation dates once the GeneXpert instrument(s) have been released by customs. Installation dates will take into account travel time to sites (and between sites if consecutive installations are to take place). The GeneXpert Focal Person (or a delegated person) and the implementing partner technical advisor should be present during installation.

INSTALLATION SITE VISIT AND CHECKLIST

During installation, the GeneXpert Focal Person or the implementing partner technical advisor should follow and complete the Installation Checklist (**Annex 2**). The Installation Checklist is used to ensure the GeneXpert instrument is installed in accordance with predefined standards and that all the relevant documentation is in place. The checklist is also used to collect relevant GeneXpert instrument data that will be uploaded to the Xpert MTB/RIF Tracking Tool (*see Monitoring & Evaluation*). The RTRL Cordinator/Appropriate Laboratory Person, Laboratory manager and Xpert users will receive a copy of the checklist with a list of non-conformances. They are responsible for implementing all additional materials and correcting the non-conformances within three months of receiving the list.

A brief narrative report must be submitted to the NTP for each installed site or group of installed sites.

PHASE 4: EARLY IMPLEMENTATION

Policy and objectives:

- The NTP, in coordination with implementing partners, will conduct regular visits and coordinate additional support to sites during early implementation to ensure Xpert MTB/RIF testing is successfully established as part of routine operations.

During installation, each module in the GeneXpert instrument should be evaluated and declared "fit for purpose" through verification with known positive and/or negative material prior to commencing testing of clinical samples. A successful installation will be supported by a qualification report generated as proof and start of warranty contract. Within three months of installation and staff training, the NTP GeneXpert Focal Person or lab advisor from partners will oversee the evaluation of the testing site. The evaluation should be carried out by relevant supervisors utilizing a standardized checklist to ensure staff have implemented as instructed during training and installation (**Annex 2**). This includes but is not limited to the implementation of all SOPs and reporting materials. Problems will be identified and retraining carried out where necessary.

The data gathered from completion of the checklists will be used to update the Xpert MTB/RIF Tracking Tool (*see Monitoring & Evaluation*). Samples submitted by the clinical sites will be tested using the Xpert MTB/RIF test and following the diagnostic algorithm. Testing sites report the Xpert MTB/RIF test results to the clinicians, and cases identified as TB & MDR- TB are treated or referred to the MDR-TB Initiation Centre (Designated Laboratory Person is responsible for the transfer of cases to the MDR-TB Unit). In the early stages of implementation, the GeneXpert Focal Person and the implementing partner technical advisors will work closely with testing sites to ensure quality of results through certain standards:

- Testing sites must be mentored and regular supervisory visits must be arranged;
- Additional training for supervisors/advanced users in troubleshooting and on-site supervision must be arranged;
- Testing sites must establish a system for instrument calibration;
- Testing sites must enroll in an EQA Program;
- Testing sites must establish a system for regular maintenance, calibration and servicing of instruments;
- Xpert MTB/RIF test results must be monitored by establishing a system of monthly reporting and review of testing site quality indicators.

The Designated Laboratory Person & RTRL Coordinator will work closely with clinical sites to ensure:

- Clinicians are following the Xpert MTB/RIF test TB diagnostic algorithm;
- TB cases are receiving the correct treatment and being started on treatment in a timely fashion;
- Cases identified as "*MTB detected rifampicin indeterminate*" are followed up
- Cases identified as *RR-TB* are referred to the MDR-TB Unit by the MDR focal person at the district or regional level and directly coordinate by NTP;
- Clinical sites are recording and reporting case detection.

EARLY IMPLEMENTATION PROGRAM EVALUATION

A program evaluation at the end of the early implementation phase ensures that the processes and systems established are functional and that implementation is able to proceed to routine testing independently of external support. Evaluation protocols should be prepared by implementing partners in close collaboration with NTP and the GeneXpert Focal Person and submitted for appropriate ethical review. The results of the assessments will be reviewed by the NTP and LWG. An annual meeting will be organized as budgeted to share findings, challenges. The outcome, measures, and scope of the evaluation must be pre-determined and should be focused on the impact of Xpert MTB/RIF test implementation on patient care and treatment results as major, important outcomes.

GENEXPERT INSTRUMENT HANDOVER

Handover of instruments, changing roles, and/or withdrawal of implementing partners is coordinated by the NTP and the implementing partner. Handover of GeneXpert instruments to the NTP can be guided by following the requirements in the Pre-Handover Checklist (**Annex 3**). The GeneXpert Focal Person or implementing partner will complete the checklist in the month before the intended handover. The checklist is used to determine the details of when, where, and what kind of Gene pert instrument was installed, what the status of calibration is; and whether all documentation

related to the GeneXpert instrument has been supplied to the NTP. The implementing partner is responsible for ensuring that the GeneXpert instrument is in good working order, and that calibration has been performed. The data gathered by completion of the Pre-Handover Checklist will be used to update the Xpert MTB/RIF Tracking Tool (*see Monitoring &Evaluation*).

PHASE 5: ROUTINE TESTING

Policy and objectives:

- The NTP will put in place procedures to maintain quality assured and uninterrupted services at all testing sites;
- The NTP will review programmatic data on a regular basis to inform program operational planning;
- The NTP will update the guideline according to new developments in the field and review any new data pertaining to TB diagnosis for possible implementation.

The routine testing phase is the concluding phase of Xpert MTB/RIF test implementation. In the routine testing phase, the NTP maintains the systems established in the earlier phases. During this phase, the NTP has to ensure that the following activities are implemented:

- Regular on-site supervisory visits according to agreed schedules using standardized checklists, conducted by the Lab Focal Person and/or Medical Officer In charge;
- Routine monthly reporting and review of testing site quality indicators, conducted by the Gene pert Focal Person Point and NTP;
- Testing site data are collated using the Xpert MTB/RIF Tracking Tool;
- Participation and review of results from the Xpert MTB/RIF test EQA Program ;
- Regular maintenance, calibration and servicing of instruments ;
- Follow-up training for testing and clinical sites; and re-training of personnel;
- Regular program evaluations to assess the impact of Xpert MTB/RIF test implementation.

GENEXPERT INSTRUMENT WARRANTY AND CALIBRATION

GeneXpert instruments purchased from Cepheid have a two-year warranty that begins from the date of shipment of the instrument. The date of shipment should be communicated to the GeneXpert Focal Person and recorded in the Xpert MTB/RIF Tracking Tool (*see Monitoring & Evaluation*) to allow for accurate forecasting.

Care will be taken to minimize shipment time by ensuring all documents required for tax exemption and customs clearance are in place before shipment is made and by regularly following up with the shipment and clearance company. Installation should take place as soon as possible to ensure the longest possible warranty coverage. To minimise delays, additional items (e.g. UPS) should be in place before instrument installation.

A one-year warranty is included in the purchase price of the instrument. The second or third year extended warranty is only valid if the GeneXpert instrument was registered on installation and the calibration was completed within one year of the shipment date. Implementing partners are encouraged to buy the extended warranty when procuring GeneXpert instruments. The warranty covers all breakdowns of the GeneXpert instrument, computer, and associated items. Within the warranty period, the implementing partner or the Gene pert Focal Person can report all breakdowns directly to Cepheid technical support. The following details should be included, where possible, in communication with Cepheid technical support:

- The serial number of the instrument
- The serial number of the computer
- Contact person (with mail, postal address, and telephone or Fax)
- The site shipment address

- The IQ report of the instrument
- The system log report for at least the last 3 months
- The last 3 months testing files in .gxx format
- The last calibration report if appropriate

Cepheid will allocate a reference code to the case; this should be used in all communications with Cepheid about this case. If troubleshooting is unable to solve the problem, Cepheid will ship a new part directly to the shipment address. A qualified authorized person (Super User) should be contacted in country to make the necessary repairs when the parts arrive. The GeneXpert Focal Person should be kept in copy for all communications with Cepheid. Calibration should be done once yearly or after 2000 tests (whichever comes first). If a module fails calibration it should not be used for further testing. The module can be isolated in the GeneXpert software. Replacement parts should be ordered from Cepheid as soon as possible. The GeneXpert Focal Person should be informed about all calibrations and the calibration report from Cepheid must be provided within one week of calibration. If modules have failed, a plan for replacing modules should also be submitted and the GeneXpert Focal Person included in all related communications.

RECORDING AND REPORTING

The new standardized reporting and reporting formats released by the WHO capture GeneXpert information (**Table 19**) and will be disseminated to all facilities in Bangladesh. This will, however, be updated when the ULTRA cartridge is introduced in the Xpert network in Bangladesh, according to the newly released guide (WHO, March 2017).

These reports include revised quarterly reports, TB Laboratory Registers, patient registers, treatment cards, testing site request forms, presumptive TB registers, and MDR registers. Xpert MTB/RIF test-related information will be integrated into the existing TB reporting structures and protocols. All testing sites are required to contribute to quarterly reports for the NTP. Xpert MTB/RIF rifampicin resistant results will be reported directly to the GeneXpert Focal Person. The data will be used to update the Xpert MTB/RIF Tracking Tool (*see Monitoring & Evaluation*).

Table 19. Approved NTP Xpert MTB /RIF results reporting codes

GeneXpert result	WHO reporting code
MTB not detected	N
MTB detected rifampicin resistance not detected*	T
MTB detected rifampicin resistance indeterminate*	TI
MTB detected rifampicin resistance detected*	RR
Error/ No result/ Invalid	I

*All MTB detected results should be written in red ink

Procurement and Supply Chain Management

FORECASTING

Policy and objectives:

- The NTP, in coordination with implementing partners, will procure quality reagents, items and services economically from reliable sources;
- The NTP, in coordination with implementing partners, will estimate, position, and monitor appropriate levels of stocks based on estimated needs, operational policy, objectives, and priorities;
- The NTP, in coordination with implementing partners, will ensure timely procurement and distribution of supplies to enable uninterrupted testing at all sites following the national algorithm.

The NTP will incorporate procurement plans for GeneXpert instruments and necessary consumables into its annual forecasting and quantification exercises for all TB laboratory diagnostic supplies and commodities. Cepheid does not provide some of the supplies required for using the Xpert MTB/RIF test. When calculating orders of supplies, past consumption rate, stock on hand, shelf life of the ordered material, lead-time, and storage capacity will be considered in order to assess quantity and frequency of orders. The Xpert

MTB/RIF test implementation plan with forecasted quantities and budget details should be aligned with the *National TB Laboratory Strategic Plan*. Implementing partners should consult with the NTP as regards procurement and placement of GeneXpert instruments and the supply of reagents through non-NTP supply chains. Specifications for additional equipment (*e.g.* Uninterrupted Power Solutions and other consumables) can be obtained from the GeneXpert Focal Person.

PROCUREMENT

There are many different channels by which Xpert MTB/RIF test cartridges are procured and supplied in Bangladesh, leading to challenges with under- and over-stocking. Distribution of cartridges to sites with GeneXpert instruments requires special consideration, as the cartridges have short shelf life. Hence, the national and regional TB control program should coordinate the distribution from a single, central point.

A national pool, under the oversight of the GeneXpert Focal Person, has been established to supply patient testing sites in the country (clinical research and privates sites are excluded as they operate independently). The monthly indicators (see *Monitoring and Evaluation section*) will be used to calculate district consumption and the appropriate allocation of supplies, including a buffer stock through GX Alert and supply monitoring tool for non-connected sites. Due to transport issues to some sites, it may be necessary to implement a district-level stock buffer to ensure stock-outs do not occur.

STORAGE AND DISTRIBUTION

A framework for the proposed Xpert MTB/RIF and upcoming new ULTRA cartridge supply chain system will be established as follows:

1. Sites send regular stock order requests to the central warehouse quarterly. To avoid stock-outs due to delivery delays via the District Manager (Civil Surgeon), the testing site should have a minimum of one month's buffer stock on hand. Emergency requests can be made under special circumstances, though frequent emergency orders should be investigated, and corrective and preventive actions taken.
2. The District Manager (Civil Surgeon) checks orders against indicators and confirms request.
3. NTP focal person confirms request by checking orders against indicators.
4. PSM unit should monitor carefully - both electronic records and regular stock counts. Reagents/consumables should be shipped in a timely fashion.
5. The NTP and the PSM unit work in close collaboration to order reagents from GDF twice per year and ensure buffer stock available at central store.

REPORTING

All testing centers must establish strong, transparent, and reliable commodity management systems at the institutional level. A system for regular inventory of cartridges must be in place with up-to-date information on stock levels and expiry dates for all available batches of cartridges. The principle of First-Expiry-First-Out (FEFO) should be strictly followed. In situations where a potential over or under-stocking occurs at testing sites, the GeneXpert Focal Person should be informed and will work with sites to transfer cartridges to other sites (to avoid expiration of cartridges) or to arrange urgent delivery of cartridges. However, this should be viewed as a last resort, and sites should be assisted in implementing an effective stock management system. The proposed framework will include the RLT/DLT and the pharmacists among the designated representatives to check orders and report errors. When available and fully functional, the supply chain for Xpert MTB/RIF will be integrated into the GX Alert and the National Logistics Management Systems. The GeneXpert Focal Person will oversee the integration process of the LIS with the NTP. The NTP & CMSD will procure in line with the approved supply plan (*Framework detailed in the Budget* line above (**Table 12**).

MAINTENANCE AND TROUBLESHOOTING OF GENEXPERT INSTRUMENTS

Policy and objectives:

- All testing sites will follow standardized procedures for troubleshooting, repair, and maintenance of GeneXpert instruments;
- The Xpert focal person is designated as the point of contact for all servicing and repair communications with the manufacturer

A number of maintenance procedures must be followed regularly (daily, weekly, monthly, and annually) according to the manufacturer's instructions to ensure proper functioning of the GeneXpert instrument, with each task checked during supervisions (**Annex 2**). GeneXpert Users are responsible for all instrument maintenance.

The extent to which users have performed instrument maintenance will be reviewed during supervisory and troubleshooting visits. Failure to maintain the GeneXpert instrument can lead to testing errors and instrument breakdowns.

GeneXpert instrument: All testing sites experiencing GeneXpert instrument failure or module failure (i.e. high errors on module, red light on the module or stuck cartridge, fan failure, communication problems) will immediately notify the Partner Local lab advisor and GeneXpert Focal Person. The GeneXpert Focal Person will contact the site and will begin troubleshooting by telephone. If the problem cannot be solved, the GeneXpert Focal Point for that region will be sent as soon as possible (within two weeks) to provide technical assistance. The Supervision Checklist **(Annex 2**) will be used to document & report the findings of the supervisory visit. The GeneXpert Focal Point will collect the following information for further examination:

- The serial number of the instrument
- The serial number of the computer
- Contact person
- The site shipment address
- The IQ report of the instrument
- The system log report for at least the last 3 months
- The last 3 months testing files in *gxx* format

The implementing partner or GeneXpert Focal Person is responsible for communicating with Cepheid, and the GeneXpert Focal Person must be copied on all trouble shooting communications. The GeneXpert Focal Person and implementing partners are responsible for following up corrective actions and evaluating their success.

Computer malfunction: All testing sites will have updated antivirus software installed on the GeneXpert computer, and the use of memory sticks, other devices, and the installation of other software on that computer is prohibited. The GeneXpert Focal Points are responsible for keeping the anti-virus software up to date. If computer-related problems are experienced, users and/or laboratory managers should bring these to the attention of their facility's information technology department. If the information technology department cannot resolve the malfunctions, the relevant Designated Laboratory Person should be contacted, who can liaise with the GeneXpert Focal Person and implementing partners to resolve the problem and/or contact Cepheid. The following information should be collected where possible for troubleshooting purposes:

- The serial number of the instrument
- The serial number of the computer
- Which windows version is on the computer
- Which software version is on the computer
- Contact person (mail, telephone)
- The site shipment address
- The IQ report of the instrument
- The system log report for at least the last 3 months
- The last 3 months testing files in *gxx* format

The implementing partner or GeneXpert Focal Person is responsible for communicating with Cepheid, and the GeneXpert Focal Person must be copied on all trouble shooting communications. The GeneXpert Focal Person and implementing partners are responsible for following up corrective actions and evaluating their success.

Xpert MTB/RIF cartridges: Damage and inappropriate use or storage of cartridges can all lead to high rates of invalid results. Upon obtaining multiple invalid results, the operator should record the batch number. If a pattern is detected (high rates of invalid results linked to a particular batch number), they must report it to their Designated Laboratory Person who may consult the GeneXpert Focal Person.

Staff-related errors: The most common GeneXpert instrument & Xpert MTB/RIF test errors are due to incorrect processing of samples. A high error rate (in particular of errors 2008, 5006, and 5007) spread across all modules suggests that operator error may be a cause and onsite re-training of staff may be necessary. RTRL Coordinator or GeneXpert Focal Points should compile a list of recommended candidates for re-training, in addition to new personnel. The list should be communicated to the GeneXpert Focal Person to arrange re-training. Preferably, candidates should be mentored on-site to ensure that training is successful.

Troubleshooting at sites (including calibration, electrical problems with the UPS) is documented by the GeneXpert Focal Point using the Supervision Checklist (**Annex 2**). Unresolved issues are escalated to the GeneXpert Focal Person for further investigation and resolution. An Authorized Service Provider (ASP) is an agency tasked by Cepheid to provide installation, troubleshooting and support to Xpert MTB/RIF testing sites on their behalf. NTP will establish contracts with the ASP. The terms of reference for the ASP will be clearly defined, and the extent of the services offered by the ASP will be communicated to the GeneXpert Focal Person. All installations and troubleshooting involving the ASP will be coordinated by the GeneXpert Focal Person.

TRAINING AND COMPETENCY ASSESSMENT

A standardized training curriculum, based on the Global Laboratory Initiative (GLI) Xpert MTB/RIF test training package (http://www.stoptb.org/wg/gli/documents.asp?xpand=2), has been customized for training of clinical and testing site personnel. The NTP will facilitate the introduction of this training manual in the Xpert network. All users must be trained using the approved national training curriculum. A cadre of master trainers will be utilized from previously trained RTRL Coordinator (for clinical training), lab advisors from partners, and the NTP GeneXpert Focal Point (for Xpert MTB/RIF test users) to provide training in all districts. The master trainers assist the NTP to cascade clinical and Xpert MTB/RIF test training in a phased manner alongside instrument placement. Additional implementing partners and the GeneXpert Focal Person can organize training according to the annual plan. Implementing partners will coordinate and report the outcome of training with the GeneXpert Focal Person. Implementing partners are responsible for the initial training of users at their testing sites, using the standardized training curriculum.

The outcomes of trainings and mentorship are recorded using the Xpert MTB/RIF Tracking Tool (*see Monitoring & Evaluation*) and a report must be provided to the NTP in a standardized narrative format.

TRAINING CURRICULUM

The standardized training curriculum revised by GLI in 2017 provides training for:

GeneXpert Users: The objective of the user training is to enable testing site personnel to perform the Xpert MTB/RIF test, understand the testing algorithms, interpret Xpert MTB/RIF test results, maintain the GeneXpert instrument, and supply the NTP with relevant quality indicators. Administrative users are the main site contacts. They are specifically trained to perform reporting functions. Users who fail to pass both theoretical and practical competency assessments can be followed up and reassessed before re-training.

GeneXpert Focal points: This training is intended for administrators and senior Xpert MTB/RIF users who have a proven track record and who have been selected to mentor other sites. The objective of the Focal point training is to enable selected testing site personnel to coordinate GeneXpert implementation activities such as supervisory visits, competency assessments, troubleshooting, and training and to collect quality indicators in country. After completing the training, GeneXpert Focal Points will be mentored by existing master trainers. This may include being supervised

during testing site assessments and GeneXpert installations as well as learning to organize and facilitate user training. After GeneXpert Focal Points graduate from the mentorship program, they will be considered *"master trainers"*.

Clinical staff: The objective of the Clinical training is to instruct clinicians and healthcare workers in the fundamentals of the GeneXpert technology, introduce the testing and treatment algorithms and to provide guidance on the requesting and interpretation of Xpert MTB/RIF test results. Clinical staff from relevant entities within the GeneXpert facility, TB unit, CTC, as well as out cases, wards, administrative staff, and staff from peripheral sites who will refer samples to the GeneXpert site, must be included in the training.

RTRL Coordinator: The objective of this training is to instruct Regional TB clinicians in the fundamentals of the GeneXpert technology, introduce the testing and treatment algorithms, and provide guidance on the requesting and interpretation of Xpert MTB/RIF test results, especially on complicated cases. This training prepares RTRL Coordinator clinicians to train clinical staff on Xpert MTB/RIF testing and to perform quarterly supervisory visits while supporting GeneXpert Focal Points. RTRL Coordinator are also trained in the collection of programmatic quality indicators.

TRAINING IN THE IMPLEMENTATION PHASES

Clinical sites:

- Following installation, the RTRL Coordinator/Designated Laboratory Person will arrange for the GeneXpert Focal Person/ or the implementing partner technical advisor to sensitize clinical staff the utility of the Xpert MTB/RIF test. Sensitization should include an introduction to the National TB Diagnostic Algorithm, sample collection and transport, as well as interpretation and reporting of results.
- It is mandatory that clinicians, TB care nurses, TB and HIV program officers, and hospital administrators undertake technical training on the Xpert MTB/RIF test use and diagnostic algorithm prior to implementing the Xpert MTB/RIF test service. 2-day training should be conducted for clinical staff using the nationally standardized training material.
- A one-day on-site sensitization workshop will be conducted for general health care workers from testing and sample referring centers, on the proper implementation of GeneXpert services, diagnostic algorithms, testing site networking, sample referrals and result feedback mechanisms.

Testing sites:

- Following installation, the RTRL Coordinator/Designated Laboratory Person will arrange for the GeneXpert Focal Person/ or the implementing partner technical advisor or Authorized Service Provider (ASP) to sensitize testing site staff to the operation of the GeneXpert instrument.
- GeneXpert users will receive technical training on the Xpert MTB/RIF test and diagnostic algorithm prior to implementing the Xpert MTB/RIF test service.
- Five-day training should be conducted for testing site personnel from Xpert MTB/RIF testing sites, using the nationally standardized training material.
- During the early implementation phase, additional training on the use of monitoring and supervision checklists is given to the GeneXpert Focal Points, testing site coordinators and RTRL Coordinator. This enables the trainees utilize the checklist during supervisory visits in their catchment areas.

Advocacy shall be targeted the inclusion of the standardized training for Xpert MTB/RIF as microscopy into the curricula of Bangladesh educational and training institutions responsible for training testing site technicians.

QUALITY ASSURANCE

Policy and objectives:

The NTP, in collaboration with implementing partners, will ensure all Xpert MTB/RIF testing sites provide quality-assured testing services according to best practices;

- The NTP will sensitize and provide training materials to all implementing partners on the approved national program for quality assurance;
- The NTP, via the GeneXpert focal person, will receive regular reports from all testing sites regarding the quality of testing (QA procedure logs, proficiency test results and quality indicator reports);
- The NTP, NTRL (or delegated regional personnel) will conduct supervisory visits to testing sites to verify quality of testing and provide support;
- All sites shall be registered for and undertake regular EQA as part of GeneXpert quality assurance.

To ensure quality results which are accurate, reproducible and timely, a comprehensive and standardized quality assurance system will be implemented in all clinical and testing sites providing Xpert MTB/RIF testing services in Bangladesh:

- Support for sites in implementing all the requirements for quality assurance will be given by the GeneXpert Focal Person, and implementing partners, and is a critical element to be covered during on-site supervisory visits.
- Quality assurance is just one part of a Laboratory Quality Management System, required to ensure quality of all a testing site's processes. Continuous quality improvement is a critical concept to be adopted by clinical and testing sites.
- Quality assurance activities for the Xpert MTB/RIF test should be integrated with quality assurance for TB smear microscopy and/or other testing, where possible.
- Quality assurance is part of the routine workload and is not a separate activity. All quality assurance activities must be documented using standardized forms. Feedback to testing sites and implementing corrective and preventive measures are the most critical aspects of any quality assurance program. Quality assurance is needed whether Xpert MTB/RIF testing is performed at a testing site or a research site.

UTILIZATION OF GENEXPERT STANDARD OPERATING PROCEDURES (SOP)

To ensure consistent implementation of quality, the GeneXpert Focal Person at the NTP and all implementing partners' lab advisors will ensure harmonization of all SOPs, documentation and forms.

Compliance with national SOPs and algorithms will ensure standardization, in particular for biosafety, collection and transportation of sputum samples, test procedures, results interpretation and reporting, database management, maintenance, troubleshooting, quality assurance, and supplies management. Refer to (**Annex 3**) for a list of documents and tools and specific SOP considerations to be followed at all testing sites.

SUPERVISORY VISITS

The GeneXpert Focal Person, and implementing partner technical advisor in co-ordination with the RTRL Coordinator, performs clinical site assessments using standardized checklists (**Annex 1, and 2**).

Clinical sites: The Designated Laboratory Person, RTRL Coordinator and/or GeneXpert Focal Points will responsible for conducting regular supervisory visits to clinical sites in their region. Clinical supervisory visits will be documented using the Clinical Checklist (**Annex 2**). All clinical sites will initially receive quarterly supervisory visits, and those performing well will be visited less frequently. Supervisors will complete a standardized questionnaire during the visit, which will highlight problems and recommendations that will be returned to the site. Existing troubleshooting channels will then be utilized (*i.e.*, follow-up intervention visits). A brief narrative report of supervisions conducted must be compiled and submitted to the NTP on a quarterly basis.

Testing sites: The following checklists will be used during supervisory visits in the early implementation phase (**Annex 2**): comprehensive, supervision, quarterly, pre-handover checklists. Supervisors undertaking testing site monitoring and supervision visits on behalf of the NTP to assess Xpert MTB/RIF test implementation use these checklists. Comprehensive site visit assessment will be conducted as an initial assessment of site competency after installation, and annually thereafter. All testing sites will initially receive quarterly supervisory visits by the GeneXpert Focal Person, Designated Laboratory Person & RTRL Coordinator and/or designated GeneXpert Focal Point. Testing sites that are performing well can be visited less frequently. Supervisors will complete a standardized questionnaire during the visit, which will highlight problems and recommendations that will be provided to the site. Existing troubleshooting channels will then be utilized (*i.e.*, follow-up intervention visits). The data gathered by completion of the checklists will be used to update the Xpert MTB/RIF Tracking Tool (see monitoring & evaluation). A brief narrative report of supervisions conducted must be compiled and submitted to the NTP on a quarterly basis.

Testing sites that are do not regularly submit quality indicator data and/or have high error/invalid/no results rates will be prioritized for additional support and retraining if necessary. Additional support and re-training is coordinated and performed by the GeneXpert Focal Person or implementing partner's lab advisor.

EXTERNAL QUALITY ASSURANCE

As WHO had not yet recommended any policy on EQA of Gene Xpert, NTP has not adopted any decision regarding this. An M & E plan with quality indicators is under implementation and was included for expansion in this implementation plan.

MONITORING AND EVALUATION (M&E)

Monitoring and evaluation of Xpert MTB/ RIF implementation is necessary to ensure the effective and efficient use of resources and also to measure the impact of Xpert MTB/RIF in order to guide and justify further scale-up. A robust monitoring and evaluation system includes appropriate indicators and support for data collection, reporting, and analysis.

In addition, it is especially important to monitor the effects that GeneXpert can have on treatment initiation rates and reduced treatment time. Assessment of these effects requires a system that can link testing site and clinical site data. M&E of Xpert MTB/RIF test implementation activities are coordinated by the GeneXpert Focal Person centrally, at the NTRL/NTP.

During the early implementation phase, many of the roles for the rollout will not have been defined, and the GeneXpert Focal Person in conjunction with the implementing partner will be responsible for collecting site data. However, in the routine testing phase, the responsibility for collecting monthly data becomes the responsibility of the RTRL Coordinator. The RTRL Coordinator and the GeneXpert Focal Points communicate directly with site supervisors, users, clinical and health care workers who in turn collect the required data from registers, logs and the GeneXpert instrument. Site data will be analyzed locally, for trends that may inform operational decisions and centrally to provide an overview of implementation at country level. The GeneXpert Focal Person must report the findings of on-going implementation to the NTP and provide feedback to sites through the reporting structures.

PROGRAMMATIC AND CLINICAL QUALITY INDICATORS

To understand the impact of the Xpert MTB/RIF test on case detection, the management of cases, and other testing site processes, additional data needs to be collected from clinical sites at the district or treatment-facility level. The quality indicator data that will be collected, analyze and reported monthly from testing sites is listed in (Annex 2 and Table 20). Other aspects of implementation, in particular data on cost-effectiveness and the impact on diagnostic delays and time to treatment initiation, are best evaluated by operational research studies rather than as part of the routine M&E.

Testing Site Quality Indicators

Testing site M&E ensures established diagnostic algorithms are being followed, detects whether a particular instrument module is functioning sub-optimally or whether any users require additional training, and allows supplies to be effectively managed.

This will allow guidance on any actions that need to be undertaken to improve effectiveness, efficiency or user performance, and to strengthen the supply management process to prevent stock- outs or cartridges from expiring by exchanging cartridges among sites. Collection of the quality indicator data can be facilitated by using a GeneXpert Remote Monitoring solution.

The quality indicator data that will be collected, analysed & reported monthly from testing sites is listed in Table 20. Collection of the quality indicator data can be facilitated by using a Gene pert Remote Monitoring solution.

Data to collect

Table 20: Laboratory quality indicators for Xpert MTB/RIF M&E Plan

Xpert MTB/RIF results	
# Xpert MTB/RIF tests MTB-	# error results
# Xpert MTB/RIF tests MTB+ RIF sensitive	# invalid results
# Xpert MTB/RIF tests MTB+ RIF resistant	# no result
# Xpert MTB/RIF tests MTB+RIF indeterminate	
Total numbers	
# total Xpert MTB/RIF tests	# total Xpert MTB/RIF tests MTB+
# total successful Xpert MTB/RIF tests	# Gene pert modules in use
# total unsuccessful Xpert MTB/RIF tests	
Analysis	
Error rate	Xpert MTB/RIF - MTB positivity rate (Xpert MTB/RIF MTB positive/all successful Xpert MTB/RIF tests)
Invalid result rate	Xpert MTB/RIF - RIF resistant rate (Xpert MTB/RIF MTB+RIF resistant/all Xpert MTB/RIF MTB positive)
No result rate	Maximum Xpert MTB/RIF testing capacity per month at this site (no. tests)
Total unsuccessful test rate	% Maximum instrument capacity being utilized

In addition, these data may be further disaggregated according to the categories of populations eligible for Xpert MTB/RIF testing and data collected on the request forms. Categorizations may be as follows:

- Presumptive new TB cases
- Presumptive TB cases living with HIV
- Presumptive TB cases who are less than 15 years old (children)
- Presumptive extrapulmonary TB cases
- Presumptive previously treated TB cases

- The number and types of various errors. Identifying the most frequent types of errors can help troubleshoot the process, given that certain errors may be associated with the technique used to process samples; other errors may be related to mechanical problems with the instrument's modules or other issues, such as room temperature
- The number of errors occurring by instrument module. If a particular module produces more errors over time compared with other modules, it may require repair
- The number of errors occurring by user. If a particular user has an unusually high number of errors, further investigation of the specific error types is warranted, since some errors may be caused by the technique used to process samples
- The number of tests lost due to power outages or surges

- The number, duration, and causes of routine interruptions in the Xpert MTB/RIF testing service. Common causes of service interruptions include cartridge stock-outs, expired cartridges, no staff available, instrument breakdown, and computer breakdown
- The number of instrument modules not functioning and the duration (in days) of module failure during the reporting period
- The number of instrument modules overdue for calibration at the end of the reporting period

Monitoring supply management:

- The number of cartridges in stock at the beginning of the reporting period
- The number of cartridges received during the reporting period
- The number of cartridges used during the reporting period
- The number of cartridges in stock at the end of the reporting period
- Whether there were any stock-outs during the reporting period, the duration of stock- out (in days)

Sources of data:

- Main laboratory record keeping (laboratory request form (DR-TB 06), Monthly report form (DR-TB 10A & 10B), laboratory register (DR-TB 05))
- WHO standardized reporting framework for TB
- An MS Excel-based data collection tool (Xpert MTB/RIF Implementation tracking tool) has been developed to collect site level data on Xpert MTB/RIF quality indicators, site supervision, training and instrument usage. Data collection will be coordinated by NTP Xpert focal person, with reporting to National TB Program on monthly basis.

XPERT MTB/RIF TRACKING TOOL

NTP Bangladesh planned to install the GxAlert in 39 machines in 2016 with the support of the Challenge TB Bangladesh Project. As of now, 25 machines have been covered for GxAlert. Remaining machines will be covered by June, 2017. The onsite training has been provided to the staff of respective centers. Currently GxAlert captured the data of the 10A form as approved by NTP. Data have been analyzed by the program people at district, regional and central level routinely and provide feedback on GeneXpert functionality, maintenance, inventory management to the respective centers. Also, this system helps to track the enrollment of diagnosed TB and DR-TB patients. Further scale up of GxAlert beyond 39 machines has not been decided. There is a need to integrate GxAlert data with the DHIS 2 system, e-TB manager and LIMS. NTP Bangladesh has not faced any major challenges to install this software, but a lot needs to be done for the sustainability of the system.

RESEARCH

The NTP will work with all partners, national research, and academic institutions to build the agenda of operational research in Bangladesh. Research on GeneXpert impact should be directed to addressing the needs of the country and be in alignment with the strategic objectives contained in the *National TB Laboratory Strategic Plan*. Those parties introducing GeneXpert instruments into Bangladesh for research purposes should follow the guidelines above. All research protocols must be submitted to NTP for evaluation and will require ethical review by the Bangladesh medical research council (BMRC). Operational research topics include:

- Patient acceptability of patient vs. sample referrals,
- Compliance to algorithms;
- Costing of EMS and sustainability studies;
- Cost-effectiveness studies.

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ANNEX 1: CHECKLISTS:

MINIMUM SITE INFRASTRUCTURE FOR GENEXPERT INSTRUMENT PLACEMENT

The minimum requirements for GeneXpert equipment installations are as follows:

- Lockable testing site with secure windows and limited access
- Functional air conditioning able to maintain a temperature below 30°C in the area GeneXpert is installed
- Able to maintain a relatively dust free environment
- Stable, secure bench space that allows a minimum of 2 inches space around the instrument
- Stable electricity supply, with secondary back-up systems in place and reliable (i.e. starts automatically and fuel is available)
- Meet minimum biosafety practices for TB
- Linked to a TB department within the facility
- Sufficient staff to operate equipment
- Linked to TB DOT or Hospital within the local area for shipment of samples to regional or central culture and DST laboratory

List of standardized country checklist annex below

1. Pre-installation Checklist
2. Installation Checklist
3. Facility supervision Checklist
4. Operator Proficiency Testing Checklist
5. Troubleshooting Checklist
6. Checklist Clinical Linkages
7. Pre-handover Checklist

INSTALLATION CHECKLISTS

PRE-INSTALLATION CHECK LIST - GeneXpert MTB/RIF

LABORATORY PROFILE	
Date of Assessment/Audit	
Name(s) and Affiliation(s) of Assessor(s)	
Laboratory Name:	
Laboratory contact name (s)	
District:	
Head of Laboratory:	
Laboratory Telephone:	
Regional or District coordinator	
Funding partners involved with Lab	
Main access to the sites (Road, air…)	

Laboratory Staffing Summary	Numbers and adequate for facility operations	
Laboratory scientist		
Laboratory Technicians		
Cleaner/ laboratory attendant Data Clerk		
Driver for sample transportation		
Does the laboratory have dedicated staff in the following areas		
Quality manager		
Safety officer		
Stock manager / store person		
Briefly describe the laboratory network in the region/district, how many TB diagnostic centers and treatment centers? Are there other labs with GeneXpert in the region		

Laboratory Physical Infrastructure	Comments
Does the laboratory have a lockable door and secure windows?	
Does the Laboratory have enough space including bench space to install GeneXpert and its related ancillary equipment	
Does the laboratory have stable power supply? – count the plug sockets available	
Does the laboratory have backup generators or solar power? Are they started manually? Is there sufficient fuel? How long does it take to start the alternate power supply	
Does the laboratory have enough appropriate chairs and benches for testing and at reception (liquid impermeable and chemical resistant?	
Does the laboratory have sufficient storage space for all consumables in temperature controlled environment (2-30°C)?	
Does the laboratory have adequate waste disposal for infections materials? Describe below	
Laboratory Environment	
Does the laboratory have a means of controlling temperature between 2-30°C e.g. air circulation, thermometers, and refrigerators? What is the normal temperature?	
Review laboratory workflow and determined appropriate location for GeneXpert, computers and accessories	
Does the Laboratory have enough wash basins with soap dispensers?	
Does the laboratory have other large, electronic and or computer based equipment?	
Does the laboratory have enough regular supply of PPE (gloves, masks, goggles)?	
Does the laboratory have refrigerator for storing sputum samples?	
Laboratory Human Resources	
Does the Laboratory need additional personnel to implement GeneXpert? Specify type and number?	
Does laboratory staff have adequate computer skills for GeneXpert and reporting needs?	
Is someone responsible for computer maintenance, virus scanner updates etc.?	
Do the laboratory staff need additional training? Specify type of training.	
Describe the current supply chain	
Is the supply chain adequate?	
How long is the average lead time from ordering to receiving stock?	
Clinic/hospital readiness	
Has the National TB algorithm for Xpert MTB/RIF testing been introduced to clinicians?	
How are lab results currently returned to clinician?	
Is there an established sample transportation system from other sites to the laboratory (Describe the current system, its adequacy, efficiency and coverage)?	

Laboratory Physical Infrastructure	Comments
Is a sample referral system in place for additional testing for TB samples at referral laboratories (transportation of samples and results, schedules, triple packaging materials)?	
Are there any additional training needs for clinical staff?	
Are TB patients initiated at this site and how long does it take to initiate TB treatment?	
Have any MDR cases previously been identified at this site and how are they handled?	
Management Involvement (This maybe clinic, hospital, Academic institution, etc.)	
Is management aware of the implementation of GeneXpert at this laboratory?	
During the assessment, did the assessors meet with management to discuss the implementation of the GeneXpert and the expectations from laboratory and management (this could take place before or after the assessments)?	
Overall rating (Tick appropriate box and give reasons in the general comments section	
Not ready : **Ready- no work :** **Ready- but minor changes:** **Ready but- major change:**	
General Comments:	

INSTALLATION CHECK LIST - GeneXpert MTB/RIF

This tool is intended to be used by staff/implementing partner undertaking laboratory monitoring and supervision visits on behalf of the National Tuberculosis Control Program (NTP) to install GeneXpert equipment for Xpert MTB/RIF test implementation according to country specific instructions. The Site Pre-assessment (**annex 1** above) report should be reviewed prior to a site visit.

The Xpert Installation Checklist is used to ensure correct implementation of the Xpert MTB/RIF test. All sections must be filled with the assistance of appropriate supplementary documentation. Documents gathered must be copied to the GeneXpert focal person and the NTP in a timely fashion.

LABORATORY PROFILE	
Date of installation	
Name(s) and Affiliation(s) of who do installation (s)	
Laboratory Name:	
District:	
Head of Laboratory:	
Laboratory Telephone:	
Funding partners involved with Lab	

Equipment details			
GeneXpert serial number		Computer details (type, windows)	
GeneXpert Software details		Printer details	

Site Plan			
Support by partners ending on date		Comments	
Support to include:	Cartridges (number)	Calibration:	Technical support:
	Statistical support	Computer support	Extended warranty
	Others:		
Training of lab staff using agreed standardized training	YES NO	Certificate provided	YES NO
Training of Clinical staff completed	YES NO	Certificate provided	YES NO
Do Laboratory staff have computing skills		Level of proficiency (1 no skills, 5 programming skills)	1 2 3 4 5
Does laboratory have regular access to internet?	YES NO	Who pays for internet access	
If no internet how will monthly stats are communicated to program?			
Comments:			

DOCUMENTATION

SOP's and protocols in place				Where are documents?	Person responsible to complete
National Gene pert testing algorithm	YES	NO	NA		
Sample transport	YES	NO	NA		
Sputum collection	YES	NO	NA		
Gene pert request form	YES	NO	NA		
Waste disposal	YES	NO	NA		
Rejection criteria and recording	YES	NO	NA		
Laboratory processing protocols	YES	NO	NA		
Results reporting	YES	NO	NA		
Patient tracing	YES	NO	NA		
Initiation on to therapy	YES	NO	NA		
Reporting of RR cases to NTP	YES	NO	NA		
Collection and transport of samples for culture	YES	NO	NA		
Room and fridge t° monitoring monthly sheets	YES	NO	NA		
Error record monthly sheet	YES	NO	NA		
Back up of computer	YES	NO	NA		
Update of virus software	YES	NO	NA		

SOP's and protocols in place				Where are documents?	Person responsible to complete
Gene pert register for laboratory	YES	NO	NA		
Monthly statistics	YES	NO	NA		
Stock ordering protocol	YES	NO	NA		
Calibration ordering protocol	YES	NO	NA		
Spill protocol and spill kit in place	YES	NO	NA		
Incidence record	YES	NO	NA		
Comments					

GENEXPERT SET UP		
Place the instrument on an appropriate surface		See document "place the instrument on an appropriate surface"
Connect all the cables and UPS	YES NO NA	See document "connect all the cables and UPS"
Turn on the instrument	YES NO NA	Switch is at back of unit
Turn on the computer	YES NO NA	
Set up the local date and time on computer	YES NO NA	See document "Change time and date"
Start the software, check that the modules are "available"	YES NO NA	See document start program and module availability
Configure the Gene pert software according to English US: System Configuration, Language	YES NO NA	See Document 5: GeneXpert_DX_regional_setting
Assign instrument letter	YES NO NA	Machine 1 =A, machine 2 = B etc.; refer to document "Assign instrument letter"
Change Gene pert name to site name A,B,C,D	YES NO NA	See document "Change Gene pert name"
Import the MTB-RIF ADF (Assay Definition File)	YES NO NA	AS per document "How to import assay definition file" (also available on all MTB-RIF CD)
Set up yearly archive files in export folder	YES NO NA	See document set up yearly archive files in export folder
Create a user admin account for NTP access	YES NO NA	See document "Create a User Admin Account"
Create a user admin account at least one onsite "super user"	YES NO NA	See document "Create a User Admin Account"
All other users to have a detail account and password	YES NO NA	See document "Create a User Admin Account"
Define system type configuration	YES NO NA	See document "Define system type configuration"
Set up system configuration	YES NO NA	See document "Set up configuration"
Run verification samples (1 per module)	YES NO NA	As per GLI instructions included with Gene pert
Did all samples run as expected	YES NO NA	*Refer to GLI instructions
Print installation qualification (IQ)	YES NO NA	See document IQ report
Register Gene pert with Cepheid	YES NO NA	See document IQ report
Register site with EQA if available	YES NO NA	Site details, contact and email
Print error code chapter for laboratory reference	YES NO NA	Manual, Troubleshooting (or uses POSTER)
Save PDF Gene pert manual on desktop	YES NO NA	See document "Desktop Icons"
Save quick stats on desktop	YES NO NA	See document "Desktop Icons"
Save yearly stats files on desktop	YES NO NA	See document "Desktop Icons"
Where are tools kept	YES NO NA	
Where are Gene pert and Microsoft CD's kept	YES NO NA	
Does site have rewritable CD's for back up?	YES NO NA	
If yes where are they stored		
Comments		

To be filled by the focal person for Xpert at the NTP			
Verification runs	YES NO NA		
IQ report	YES NO NA		
Contact details	YES NO NA		
Agreement of partner support document	YES NO NA		
Comments:			
Is the machine fully operational and set to country specific standards	YES NO NA		
Comments			

Conclusions:

Recommendations:

Sign Partner representative		Sign installer	
Sign NTP Xpert focal person responsible			

ANNEX 2. EARLY IMPLEMENTATION CHECKLISTS

Facility Supervision Checklist - GeneXpert MTB/RIF

Date:

Laboratory/Hospital:

Location: City/Town/ District:

Laboratory Manager and contact:

Name of partner organization provided GeneXpert support:

Name of supervisor/assessor:

The tool is intended to be used by staff/consultants (implementer's) undertaking laboratory monitoring and supervision visits on behalf of the Bangladesh NTP to assess Xpert MTB/RIF test implementation. On-site supervisory visits form a critical part of the quality assurance program associated with Xpert MTB/RIF implementation, and will be conducted at pre-determined time intervals as agreed by the NTP. Comprehensive site visit assessment will be conducted as an initial assessment of site competency after installation, and annually thereafter.

Documents available in laboratory	Check	Comments
Xpert/ Laboratory register		
Xpert/ Laboratory SOPs		
Xpert/ Service & Maintenance SOPs		
Xpert/ Operator proficiency testing and competency assessment		
National diagnostic algorithms present and posted		
Xpert Troubleshooting problem documented		
Laboratory bench job aids (posted)		

General information on GeneXpert operation in the laboratory	
Date of start of GeneXpert operation	
Total number of Xpert performed per month/quarter/year	

	YES	NO	ACTION UNDERTAKEN / COMMENTS
GeneXpert placement			
Is there adequate space for the GeneXpert machine, and computer			
Is machine placed in a clean and dust-free area? (or covered when note in use)			
Is A/C available in room and functional? (or RT monitored)			
Is machine placed opposite/away from the A/C unit?			
Is the machine placed away from direct sunlight or heating source?			
Does the machine space at the back side to exhaust for proper cooling (>5cm)?			
Electricity			
Does the machine have regular-uninterrupted power?			
All tests were run without abortion due to power cut-offs?			
Is UPS available and operational?			
Safety			
Is sputum preparation performed in a well-ventilated area			
Is personal protection (gloves, lab coats, and N95 mask) used during sputum preparation?			
Are sputum cups or Falcon tube used with a screw cap to avoid spilling of the sample during shaking process?			
Sputum collection			
Is sputum collection done at a designated sputum collection area or booth away from other patients or staff?			
Is there a sample transportation mechanism in place to send samples to the Xpert lab?			
Are sputum samples used of good quality? What % is saliva?			
What is done if the sputum quality is not good? (describe)			
Storage			
Are the cartridges kits stored at the appropriate temperature, 2-28◦C/ 2-8 ◦C			
Is the temperature recorded in the cartridge storage area daily?			
Did any cartridges kits expire this year?			
Are expired cartridges Kits discarded?			
Are stock cards or inventory records available and up-to-date?			
Was any cartridge stock-out recorded? If so, when/how long?			
Waste management			
How are used Xpert cartridges disposed? (explain)			
Is infectious waste discarded following the national guidelines?			
Staffing/human resources			
Are adequate numbers of staff trained on Xpert testing? (#)			
When was the last training performed and by who? (describe)	-	-	
Did routine Xpert operation start immediately after training? (note delay if any)			
Average number of Xpert tests performed per month	-	-	

Documentation (Xpert)			
Is the test included in the national lab register?			
Is the lab register filled correctly and completely? (Lab number, patient info, referral clinic, date of tests, Xpert result, smears)			
Are Xpert testing request available?			
Are the request forms correctly filled?			
Are Xpert results reported back to clinic within 1/4 days? (record average TAT)			
Is there an electronic data system available/regular data entry?			
Machine operation			
Number of unsuccessful tests to this date?			
Is the rate of invalid/error/no test results below 5%? (Xpert)			%:
Are error numbers recorded in lab register? (Xpert)			
Which types of errors occur most frequent? (Xpert)	-	-	

Xpert tests done in last 3 months:

Period:	All tests	DR TB	HIV /TB	Child	EPTB	UNK
Total suspects tested with Xpert						
Successful test results:						
Xpert MTB positive RIF detected						
Xpert MTB positive RIF not detected						
Xpert MTB pos. RIF indeterminate						
Xpert MTB negative						
Unsuccessful test results:						
error						
invalid						
no result						

Operator Proficiency Testing Checklist: Hands-on Procedures - GeneXpert MTB/RIF

Date:

Location of the facility: City/Town / District:

Name & contact of Laboratory/Hospital:

Name and function of evaluated operator:

Name and function of filling in this form:

Instructions:

- Supervisor fills in one form per evaluated operator.
- In the presence of the supervisor, the operator will prepare one specimen and analyze it on the GeneXpert system. No further instructions are given.
- If answer is "No", operator is re-trained on-the-spot using respective SOPs. Please indicate whether re-training was done using checkbox.

GeneXpert Laboratory SOPs	Correctly done		Retraining
	YES	NO	CHECK
Sample integrity and storage			
Sputum samples collected and transported to the lab. Appropriately			
Samples free of obvious food particles and solid particles			
Sample mix (Sputum/pellets) stored appropriately in case of delay in Xpert test			
Sputum samples stored appropriately (2-8°C) in case of processing delay; specimen stored at -20C.			
Warn personnel about necessity to defrost pellets completely before processing			
Sample preparation			
Did the operator add the correct amount of buffer to the specimen?			
Did the operator vigorously shake the specimen after adding the buffer?			
Was the specimen shaken a second time during the entire incubation time?			
Was the incubation time of 15min respected?			
Did the operator transfer the correct amount of sample to the cartridge?			
Starting the test on the GeneXpert instrument			
Did the operator start every test without any problems?			
Did the operator correctly label the cartridge with the specimen/patient ID?			

GeneXpert Laboratory SOPs	Correctly done		Retraining
	YES	NO	CHECK
Post-test procedures			
Did the operator clean & disinfect the workplace after completion of tests?			
Did the operator discard all waste in the lab-defined way?			
Was the operator able to retrieve the results from the software without any problems?			
Did the operator record and report the correct results (i.e. indicated on the software)?			

GeneXpert Software, Service & Maintenance, and Troubleshooting SOPs	Correctly done		Retraining
	YES	NO	CHECK
Software Tasks			
Can the operator enter details manually (in case the barcode reader does not work)?			
Can the operator retrieve results for all tests run in the last week?			
Can the operator retrieve results for a specific test (give sample/patient ID)?			
Can the operator perform manual self-test?			
Troubleshooting			
Can the operator view details or error number of invalid/error/no result?			
Can the operator retrieve the explanation for error numbers in manufacturer manual?			
Maintenance			
Daily			
Discard used cartridges			
Keep module doors upright			
Put the dust cover on the GeneXpert at the end of the day			
Disinfect cartridge bay interior with 1 % bleach and 70 % alcohol			
Monthly			
Can the operator perform plunger cleaning (disinfect plunger rod with1%bleach and 70% alcohol)			
Clean fan filter with water and soap			
Disinfect GX instrument surfaces with 10 % bleach and 70% alcohol			
Archive runs test with the support of the supervisor (skilled staff)			
Delete runs test with the support of the supervisor (skilled staff)			
Calibration			
Can the operator indicate correctly the date of next calibration?			

Troubleshooting Checklist: GeneXpert Instrument

Date of visit:

Location of the facility: City/Town / District:

Name & contact of Laboratory/Hospital:

Name and function of filling in this form:

This tool is intended to be used by staff/consultants (implementer's) undertaking laboratory monitoring and supervision visits on behalf of the Bangladesh NTP to assess Xpert MTB/RIF test implementation. The Troubleshooting Checklist is used to monitor on-going implementation of the Xpert MTB/RIF test. The checklist must be used for supervision site assessments, the follow-up of non-conformances from previous site assessments, and for troubleshooting when previous the quality indicators from the site indicate high failure rates or when the site reports technical problems that require an intervention.

Troubleshooting	Observations/ Comments
Who informed troubleshooting visit	
Detail any previous problems that may be relevant?	
Details of current problem	
Has CEPHEID or representative been contacted? If YES what is the CODE and who is responsible?	
Briefly describe trouble shooting already attempted and outcomes (attach communications if applicable)	
Additional comments and observations	
Conclusion and corrective actions taken on day of visit:	
Recommendations to be followed and by WHOM?	
Has problem been resolved?	YES NO NA Comment:
Is further follow up required? If so, by WHOM?	YES NO NA Comment:

Check the results files since the last visit and record up to 20 of the most recent error codes and which module they have occurred on:

Error codes	Module	Staff Name	Date

Checklist Clinical Linkages - GeneXpert MTB/RIF HIV/VCT/ART center

Date:

Name of Hospital:

Location/District, Town:

Name & function of supervisor:

Name & contact of Hospital Management:

This tool is intended to be used by staff/consultants (implementer's) undertaking clinical site monitoring and supervision visits of behalf of the Bangladesh NTP to assess GeneXpert MTB/RIF test implementation. On-site supervisory visits will form part of the quality assurance program associated with GeneXpert Xpert MTB/RIF test implementation, and will be conducted quarterly or at pre-determined time intervals as agreed by the National Tuberculosis Control Program. Ad hoc supervisory visits may also be required.

Documents available in the clinic	Check
Xpert suspect register book	
DR TB Xpert treatment register book	
Xpert test request forms (Form DR TB 06)	
Xpert diagnostic algorithms (posted)	
Sputum collection SOPs (printed)	

General information on Xpert usage	
Number of clinicians trained on Xpert guidelines	
Number of other health care workers trained on Xpert guidelines	
Date of first HIV positive TB suspect sent for Xpert testing	
Total number of HIV positive TB suspects tested with Xpert up to this date	

•If answer is "No", problems are solved on-the-spot. Please explain how the problem was solved under "Action undertaken".

	YES	NO	ACTION UNDERTAKEN
Staffing/human resources			
Are adequate numbers of clinical staff trained on national Xpert guidelines?			
When was the training performed and by who? (describe)			
Did clinicians start to send suspects for Xpert testing immediately after training?			
Average number of suspects sent for Xpert per week			
Sputum collection			
Is sputum collection done at a designated safe sputum collection area/booth/spot?			
Are suspects instructed how to produce good quality sputum?			
What is done if the sputum quality is not good? (describe)			
How many sputum samples are collected per suspects and for which diagnostic tests? (describe)			
Suspect referral			
Do clinicians send the right suspects for Xpert testing, according to national guidelines?			
How many PLHIV were on care in the clinic last year?			
What percentage of PLHIV was screened for TB symptoms and received a TB test?			
What percentage of PLHIV was TB co-infected?			
Is the correct Xpert suspect register book used?			
Is the Xpert suspect register book filled in completely?			
Are the correct Xpert test request forms (TB06)?			
Is the Xpert test result copied adequately from the test request form (DR TB 06) to the suspect register book?			
Are >90% of Xpert test results received back in the clinic within 2 days?			
Are sputum smear microscopy results filled adequately in the Xpert suspect register book?			
Clinical management			
Are all HIV positive individuals with an Xpert MTB positive result placed on first-line TB treatment?			
Is the date of treatment start completed in the Xpert suspect register book?			
If not, is start of treatment recorded elsewhere? (describe)			
Are >90% of Xpert MTB positive cases started on first-line TB treatment within 1 week?			
Are all HIV positive individuals with an Xpert MTB positive RIF resistant result referred to a nearby PMDT center?			

Summary of NO- Conformity & Corrective actions

Non-conformity	Recommended corrective action	Follow-up required

Checklist Clinical Linkages - GeneXpert MTB/RIF PMDT center

Date:

Name of Hospital:

Name & function of supervisor:

Name & contact of Hospital Management:

- If answer is "No", problems are solved on-the-spot. Please explain how the problem was solved under "Action undertaken".

Documents available in the clinic	Check
Xpert suspect register book	
Xpert treatment register book	
Xpert test request form book	
Xpert diagnostic algorithms (posted)	
Sputum collection SOPs (printed)	

General information on Xpert usage	Check
Number of clinicians trained on Xpert guidelines	
Number of other health care workers trained on Xpert guidelines	
Date of first MDR TB suspect sent for Xpert testing	
Total number of MDR TB suspects tested with Xpert up to this date	

	YES	NO	ACTION UNDERTAKEN
Staffing/human resources			
Are adequate numbers of clinical staff trained on national Xpert guidelines?			
When was the training performed and by who? (describe)			
Did clinicians start to send suspects for Xpert testing immediately after training?			
Average number of suspects sent for Xpert per week			
Sputum collection			
Is sputum collection done at a designated safe sputum collection booth/spot?			
Are suspects instructed how to produce good quality sputum?			
What is done if the sputum quality is not good? (describe)			
How many sputum samples are collected per suspects and for which diagnostic tests? (describe)			

Suspect referral			
Do clinicians send the right suspects for Xpert testing, according to national guidelines?			
How many retreatment cases were identified last year?			
Is the correct Xpert suspect register book used?			
Is the Xpert suspect register book filled in completely?			
Are the correct Xpert test request forms (DR TB 06) used?			
Is the Xpert test result copied adequately from the test request form (DR TB 06) to the suspect register book?			
Are >90% of Xpert test results received back in the clinic within 2 days?			
Clinical management			
How many beds are there in the MDR ward?			
Are all MDR TB suspects with an Xpert MTB positive RIF resistant result started on second-line TB treatment?			
Is the date of treatment start completed in the Xpert suspect register book?			
If not, is start of treatment recorded elsewhere? (describe)			
Are >90% of Xpert RIF resistant cases started on second-line TB treatment within 1 week?			
Is eTB manager available and regularly updated?			
Referral for culture and DST testing			
Are all samples/patients with Rif resistant results sent to a culture and DST laboratory?			
Are the dates of sending samples/patients for culture and DST recorded in the Xpert suspect register book?			
Is there a sample transportation mechanism in place to send samples to culture and DST laboratory?			
Are results from culture and DST laboratory send back to the clinic within 2 months?			
Are results from culture and DST recorded in the Xpert suspect register book?			
If not, are culture and DST results recorded elsewhere? (describe)			

Suspects tested with Xpert:

Period:	All suspects	MDR TB suspects*	HIV TB suspects	Unspecified suspects
Total suspects sent for Xpert				
Total suspects tested with Xpert				
Test results:				
Xpert MTB positive RIF not detected				
Xpert MTB positive RIF detected				
Xpert MTB pos. RIF indeterminate				
Xpert MTB negative				
error				
invalid				
no result				

**** Specify the number of MDR TB suspects per each of the 1-9 criteria***

Laboratory Xpert Pre-handover checklist

This document is developed by the Bangladesh NTP and its partners to facilitate transition of GeneXpert instrument, related equipment's and consumables' under MOH and NTP management at the end of project implementation for a smooth and sustain process.

PART 1. CONTACT DETAILS	
Date of installation	
Facility name/Laboratory name	
Contact details facility: Name, phone, email	
Partner organization responsible Contact details Name, phone, email	

PART2. EQUIPEMENT DETAILS			
GeneXpert serial number(s)		Number of modules	
Laptop/desktop		Brand computer	
Window version		Antivirus version	
GeneXpert software version		Battery /stabilizer details	
UPS details			
Comments:			

PART3: SITE PLAN			
Support by partners ending on date		Comments:	
Hospital or NTP to takeover (please mark as appropriate)	Cartridge supply (Average no. per month)	Calibration	Technical support
	Statistical support	Computer support	Printer/Ink/Paper
	Other:		
At handover date estimate remaining cartridges and expiry		Any other outstanding issues?	
Have all modules Passed calibration?	YES NO	Comment if any:	
Attach report; If NO and detail what follow up action is being undertaken			

Has error rate over last 3 months been below 5%	YES	NO	Attach report; If NO and explain	
Has total unsuccessful test rate been below 10%?	YES	NO	Attach report; If NO and explain	
Has Cepheid examined last 3 month system log and .gxx files?	YES	NO	Attach report; If NO and explain	
To the best of your Knowledge using all available tools is the GeneXpert machine in full working order as of hand over date?	YES	NO	Comments:	
Is this machine still under original warranty	YES	NO	Date of warranty end	
Has any extended warranty been purchased	YES	NO	Date of warranty end	
Was this site following NTP testing algorithm?	YES	NO	If NO which algorithm was used	
Was this site supplying monthly indicators to the NTP?	YES	NO	If NO, what was agreement and can staff produce monthly statistics?	
Are there any additional training needs to ensure a smooth handover	YES	NO	Detail:	
Have all staff performing testing completed and passed a certified training program for Xpert MTB/RIF testing	YES	NO	If NO detail:	
Have clinical staff completed sensitization about MTB/RIF testing	YES	NO	If NO detail:	
Are standard NTP procedures, SOPs, registers and other documents in place	YES	NO	If NO detail:	
Additional comments:				

PART 4. OTHER DOCUMENTS TO BE SUPPLIED AT HANDOVER				
Certification document	YES	NO	NA	Supplied with machine
Verification documents	YES	NO	NA	*To be decided how many and what is required
System log and last 3 months .gxx files	YES	NO	NA	As per document, how to generate a system log report and How to archive and delete runs
New IQ reports	YES	NO	NA	As per document how to generate an IQ report
Copy of last 6 months maintenance records				Copied from laboratory records, if any missing please explain below
Copy of staff training certificates for Xpert MTB/RIF	YES	NO	NA	Copied from laboratory records, if any missing please explain below
Evidence of clinical Sensitization	YES	NO	NA	Certificates, training schedule, meeting minutes
Provide a letter explaining handover to be sent to Cepheid as evidence of change of owner	YES	NO	NA	As per document
Comments:				

PART5. COMPLETION OF GENEXPERT HANDOVER	
Partner signs to declare handover of GeneXpert instrument in full working condition and has no further role apart from that documented above	
NTP signs to confirm receipt of GeneXpert machine in full working condition and takes responsibility for full site support, including reagent supply, calibration and technical support	
Comments	
Disputes:	
Further actions:	
Final handover date:	

Annex 4: SOP Considerations

The following is a list GLI/FIND installation and training documents, tools and SOPs for use with Xpert MTB/RIF testing:

Package 1 documents (provided)	Package 2 documents (in-country tools)
Xpert MTB/RIF country- specific installation checklist	TB suspect screening tool
Xpert MTB/RIF installation accompanying documents	Sputum testing national testing algorithm
Xpert MTB/RIF Manual	Sputum sample testing request form for Xpert MTB/RIF
Xpert MTB/RIF SOP	Laboratory Sample register
Xpert MTB/RIF monthly indicator reporting form	Results reporting procedures
Xpert MTB/RIF equipment maintenance SOP	Sample TAT records
Xpert MTB/RIF equipment maintenance records	Patient tracing procedure
Xpert MTB/RIF sputum sample collection SOP	Patient initiation onto treatment procedure
Xpert MTB/RIF WHO reporting codes	RIF detected reporting to National TB Program procedures
Xpert MTB/RIF error records and corrective action log	Stock ordering protocols
Xpert MTB/RIF equipment error code list	Stock cards
Xpert MTB/RIF equipment user training package	Incidence occurrence records
Xpert MTB/RIF clinical training package	Waste management procedure
Sputum rejection criteria	Sample collection for culture
	Sputum transport procedure
	Spill management procedure
	Temperature monitoring records

Consider including the following information in the appropriate SOPs.

Case Definition, Documentation and Reporting

The following information is captured in the SOP for Case Definition, Documentation and Reporting.

Based on WHO recommendations, all patients diagnosed to have TB by Xpert MTB/RIF shall be defined as a TB case:

- A bacteriological confirmed TB case: one from whom a biological specimen is positive by smear microscopy, culture, or Xpert MTB/RIF. All such cases should be notified to TB control program.
- Rifampicin resistance TB (RR-TB) case: resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether mono-resistance, multidrug resistance, poly-drug resistance or extensive drug resistance.

The new standardized reporting and reporting formats released by WHO capture Xpert MTB/RIF information and include revised quarterly reports, laboratory registers, patient registers, treatment cards, laboratory request forms, presumptive TB registers, and MDR registers. In this sense, Xpert MTB/RIF-related information will be integrated into

the existing TB reporting structures and protocols. All laboratories will be required to contribute to quarterly reports for the National TB program and Central TB Reference Laboratory. The laboratory supervisors should check and confirm statistical accuracy of the most recent quarterly reports directly from the Xpert MTB/RIF equipment during supervisory visits and compiles them for their district or region to assist with stock management and troubleshooting. Quarterly case finding should be reported by the Xpert MTB/RIF testing site while the enrolment of patients in to care should be reported by the treatment initiating centre. To facilitate this activity, the Referral Samples Logbook, Postal TB Sample Logbook and Sample Referral SOP will be used.

Xpert MTB/RIF results reported as follows:

T	MTB detected, rifampicin resistance not detected
RR	MTB detected, rifampicin resistance detected
TI	MTB detected, rifampicin resistance indeterminate
N	MTB not detected
I + error number	invalid / no result / error

Laboratory infrastructure requirements

- Uninterrupted power supply (UPS with minimum capacity of 2 hours and/or a Generator with fuel supply)
- Closed room with temperatures no higher than 30°C and Air Conditioning system in hot areas
- Closed room with temperatures not higher than 30°C and Air Conditioning system in hot areas
- Adequate storage room for cartridges with temperatures not higher than 28°C
- Secured location to protect Xpert MTB/RIF machine and computer from theft
- Adequate space for specimen receipt and preparation for testing
- At least one 2-8°C refrigerator for specimen storage as needed
- Reliable water supply with sink
- Lab chairs and desks for paper work and documentation activities

Bio-safety requirements

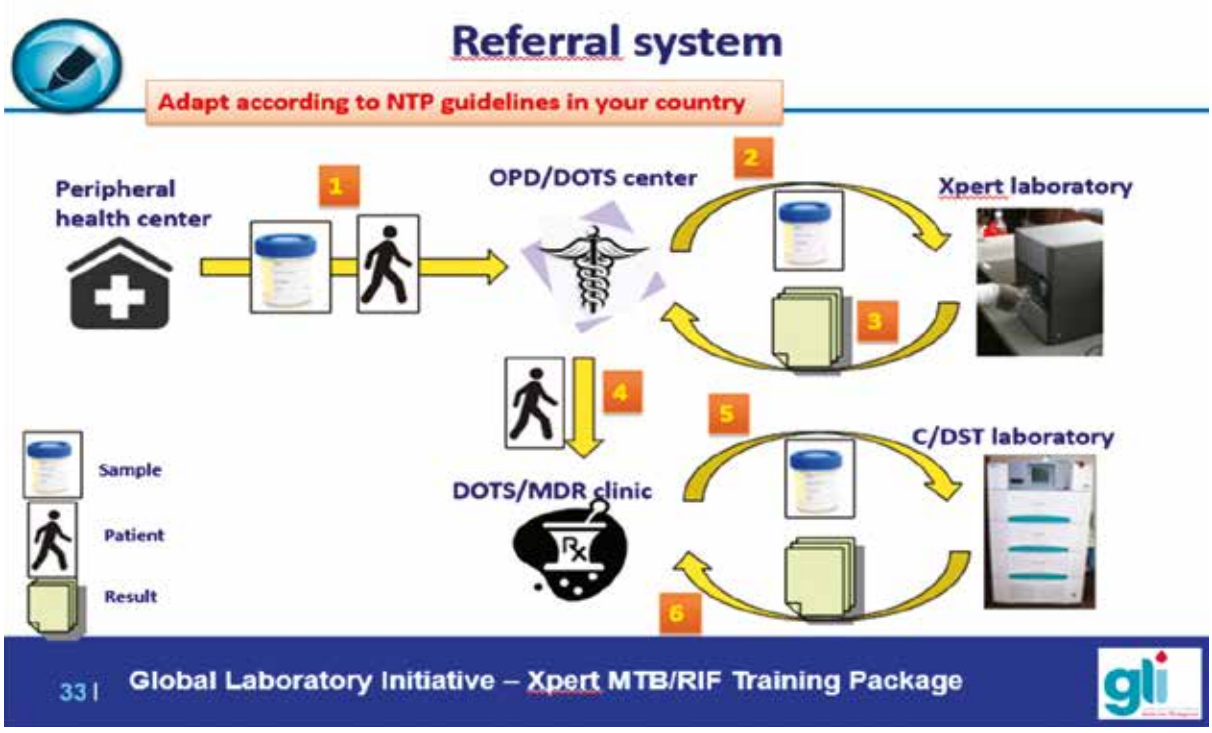
- Waste disposal system for cartridges. Example: Incineration
- Biosafety level equivalent to smear microscopy (cross ventilated room)
- Gloves for specimen handling
- Containers for triple packaging of referral specimens
- Standard laboratory safety precautions and practices must be followed

The following laboratory SOPs are required for the Xpert MTB/RIF implementation:

Sample referral system requirements

- The laboratory networking for specimen referral shall be based on geographic proximity to the Xpert MTB/RIF MTB/RIF testing centre and specimens will be transported using the current available courier system
- The available transport system [insert description here]
- The expected turn-around times: [insert description here. i.e. delivery of test results for patients from the same facility should be within same day of sample collection. Test results for samples from outside of the testing site (referral samples) should be delivered within five working days from the day of receipt]

Figure 1: Example of a Referral system (taken from GLI Xpert MTB/RIF training package)



Preventive maintenance:

Frequency	Task
Daily	• Remove and properly dispose of cartridges • Clean and disinfect work area • Ensure 10cm clearance around instrument • Put on dust cover when instrument not in use
Weekly	• Disinfect the interior of the cartridge bay • Restart the Gene pert instrument and computer
Monthly	• Disinfect plungers • Disinfect the instrument's surfaces • Clean the instrument's filter (this applies only to newer model (Gene pert instruments, which have a white cover) • Archive and back-up test results
Annually	Run XpertCheck cartridges (calibration) and swap modules if needed

Corrective Action Form

Date	Corrective Action Description and Resolution	Signature of person reporting Corrective Action	Corrective Action Completed (Y/N)	Signature of Supervisor	Date Correction Action was Completed

TRAINING ATTENDANCE LOG

Name of Training	
Location	
Date	

	Name	Institution	Title/Position	Telephone	Email	Signature
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						